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COOPERATIVE AGREEMENT NUMBER DAMD17-95-2-5015

TITLE: Effect of Oral Contraceptives, Menstrual Phase and
Conditions on Alertness, Performance, and Rhythms in Sleep
Deprived Women

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REPORT DATE: July 1996

TYPE OF REPORT: Annual

PREPARED FOR: Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

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DTIC QUALITY INSPECTED 3

19971215 027

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

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|---|---|--|--|--|
| 1. AGENCY USE ONLY (Leave blank) | | 2. REPORT DATE July 1996 | 3. REPORT TYPE AND DATES COVERED Annual (18 Aug 95 - 17 Jul 96) | |
| 4. TITLE AND SUBTITLE Effect of Oral Contraceptives, Menstrual Phase and Conditions on Alertness, Performance and Rhythms in Sleep Deprived Women | | | 5. FUNDING NUMBERS DAMD17-95-2-5015 | |
| 6. AUTHOR(S) Pietro Badia, Ph.D.; Milton Hakel; Kenneth P. Wright, Jr.; Bryan L. Myers | | | | |
| 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Bowling Green State University Bowling Green, Ohio 43403-0228 | | | 8. PERFORMING ORGANIZATION REPORT NUMBER | |
| 9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Commander U.S. Army Medical Research and Materiel Command Fort Detrick, Frederick, MD 21702-5012 | | | 10. SPONSORING/MONITORING AGENCY REPORT NUMBER | |
| 11. SUPPLEMENTARY NOTES | | | | |
| 12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited | | | 12b. DISTRIBUTION CODE | |
| 13. ABSTRACT (Maximum 200) During our first year of funding, we tested the effects of caffeine, bright light, and placebo treatments on alertness, performance, mood, melatonin, and body temperature during 48 hr of sleep deprivation. We also assessed the effects of menstrual cycle phase (Follicular vs. Luteal) and Oral Contraceptive use on the same measures. To date, 42 women have participated. These subjects were tested in one of 9 experimental conditions: Dim Light Placebo-Follicular Phase, Dim Light Placebo-Luteal Phase, Dim Light Placebo-Oral Contraceptive, Dim Light Caffeine-Luteal Phase, Dim Light Caffeine-Oral Contraceptive, Bright Light Placebo-Luteal Phase, Bright Light Placebo-Oral Contraceptive, Bright Light Caffeine-Luteal Phase, Bright Light Caffeine-Oral Contraceptive. Caffeine (100 mg) was administered orally at 2000, 2300, 0200, and 0500 hr and bright light exposure (> 5,000 lux) occurred from 2000 to 0800 hr each night. Preliminary results suggest that caffeine and bright light treatments reduced melatonin levels and enhanced nighttime alertness, performance, and temperature compared to Dim Light Placebo control conditions (< 88 lux). These results are consistent with previous findings for males tested in a similar protocol. Since the experimental conditions are only partially completed, it is too early to draw conclusions regarding treatments or the effects of menstrual phase and oral contraceptives on the various measures used (e.g., alertness, performance, etc.). | | | | |
| 14. SUBJECT TERMS Defense Women's Health Research Program | | | 15. NUMBER OF PAGES 97 | |
| | | | 16. PRICE CODE | |
| 17. SECURITY CLASSIFICATION OF REPORT Unclassified | 18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified | 19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified | 20. LIMITATION OF ABSTRACT Unlimited | |

FOREWORD

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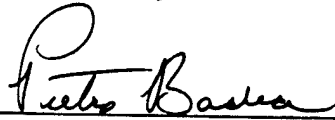
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INTRODUCTION

There is compelling evidence from both laboratory and field studies that efficiency is reduced when performance occurs out-of-phase with the normal 24-hr rest/activity cycle (e.g., night work, sustained or continuous operations, rotating shift work). Much of this lowered efficiency is due to the individual's inability to maintain alert wakefulness throughout the work period (Colquhoun 1984; Krueger 1989). The latter is especially so under conditions of sustained and continuous operations when work is required during periods normally reserved for sleep.

The present report describes ongoing research exploring methods of enhancing alertness and performance in women under sustained wakefulness conditions. Specifically, under investigation are the effects of caffeine and bright light, alone and in combination, on alertness and performance during 48 hr of sleep deprivation. The effects of these treatments on neurobiological mechanisms underlying changes in alertness and performance, namely melatonin and body temperature, are also explored. Our report addresses factors specific to women, including menstrual cycle phase and oral contraceptive use, which may affect their responses to sleep deprivation. Gender similarities and differences in psychological and physiological responses to sleep deprivation will be discussed. Lastly, the report addresses important theoretical issues that relate to the broader context of circadian rhythms.

In the work setting, nighttime productivity is reduced both in amount and quality, and accidents and errors are increased (Dinges et al. 1995; Gold et al. 1992; Horne and Reyner 1995; Lauber and Kayten 1988). Such problems are believed to be especially acute in certain civilian and military settings where lowered levels of performance, readiness, and errors in judgment can result in accidents of great consequence (Dinges et al. 1995; Gold et al. 1992; Horne and Reyner 1995; Lauber and Kayten 1988). Previous research shows performance efficiency to be related to various circadian factors (Akerstedt, 1995; Akerstedt et al. 1979; Badia et al. 1991; Colquhoun, 1984; Folkard, 1990; Krueger, 1989; Smith, 1992). For example, variation in alertness and performance across the 24 hr day is related to the circadian rhythms of the pineal hormone

melatonin and of body temperature. In general, during the early morning hours (0200 to 0600 hr) when melatonin is high and body temperature is low, alertness and performance are low. On the other hand, during the daytime when melatonin levels are low and body temperature is high, alertness and performance are high.

Melatonin is a hormone with signaling and hypnotic properties. For example, melatonin is considered the messenger of the circadian pacemaker providing photoperiod information to the organism (Reiter, 1991a, 1991b, 1991c). Ingestion of the hormone during the daytime or nighttime hours results in decreased alertness, sleepiness, and decrements in performance (e.g., Dawson and Encel, 1993; French et al., 1993; Hughes, Badia et al., 1994; Lieberman et al., 1984; Waldhauser et al., 1990). Melatonin is also involved in thermoregulation with humans as demonstrated by both correlational and experimental evidence (Badia et al., 1992; Myers et al., 1992). In general, increases in melatonin due to endogenous or exogenous sources results in decreases in temperature. Conversely, decreases in melatonin results in higher temperatures.

The circadian rhythm of body temperature correlates well with rhythms in alertness and performance. Performance and temperature both rise in the early morning, are high during the day, and trough during the hours when people would normally be sleeping. Regardless of when performance on a particular task is best, performance is almost always at its worst at the temperature trough during the early morning hours (0200-0600 hr).

Research has shown that melatonin secretion and body temperature levels can be controlled and that control of these rhythms results in control of nighttime alertness and performance (Badia et al. 1991; Lewy et al. 1980; McIntyre et al 1989; Murphy et al. 1995, 1996; Myers and Badia, 1993, Wright et al. 1995a, 1995b). Specifically, the reduction of melatonin and the enhancement of body temperature results in improved alertness and performance during sustained wakefulness. Two treatments which reduce melatonin, increase temperature and enhance nighttime alertness and performance are caffeine ingestion (e.g., Smith et al 1993; Wright et al. 1995a, 1995b) and exposure to bright light (Badia et al. 1991; Campbell

and Dawson, 1990; French and Hannon, 1990; Daurat et al. 1993; Dawson and Campbell, 1991; Horne et al. 1991; Myers & Badia, 1993; Myers et al. 1995; Murphy et al. 1995, 1996; Wright et al. 1995a, 1995b).

Despite the large amount of research conducted on the effects of caffeine and bright light on nighttime alertness and performance during sleep deprivation, no study has considered gender differences in the response to sleep deprivation. There are several factors specific to women which may influence their ability to maintain alertness and performance during sleep deprivation. First, studies have shown melatonin and temperature levels change as a function of menstrual cycle phase. Melatonin and temperature levels are highest during premenses and lowest during periovulation (e.g., Hariharasubramanian et al., 1985; Potts & Wood, 1972; Webley & Leidenberger, 1986). In addition, the use of oral contraceptives increase both nocturnal melatonin synthesis and body temperature (e.g., Arendt, 1979; Potts & Wood, 1972; Webley et al., 1985). This effect is especially true during the late luteal phase when progestin levels in the contraceptive are high. As noted, melatonin and body temperature are thought to be important factors affecting nighttime alertness and performance (Badia et al. 1991; Murphy et al. 1991; Wright, 1996). Since melatonin and temperature vary with changes in a woman's endocrine environment, women may respond differently to sleep deprivation depending upon menstrual cycle phase and oral contraceptive use. Specifically, high melatonin and high temperature levels observed during the luteal phase, in women using and not using oral contraceptives, may influence nighttime alertness and performance. It is difficult to hypothesize whether alertness and performance will be increased or decreased under these conditions. That is, because of higher melatonin levels, performance could be worse in the luteal phase for both oral contraceptive users and nonusers when compared to women in the follicular phase. On the other hand, performance could be better in the luteal phase because of higher temperature levels. The effects of higher melatonin and temperature levels on alertness and performance in women during sleep deprivation remains to be determined.

Variation in melatonin and temperature levels due to menstrual phase and oral contraceptive use may also influence the ability of caffeine and bright light treatments to enhance alertness and performance during sustained wakefulness. Specifically, higher melatonin levels may decrease the effectiveness of caffeine and bright light treatment, or higher temperature levels may increase the effectiveness of the treatments. How the combination of higher melatonin and higher temperature levels influence caffeine and bright light effects on alertness and performance during sleep deprivation remains to be determined.

Women may also respond to light differently than men due to psychological (mood) changes associated with premenses. Light therapy with bright light reduces the symptoms of depression, irritability and physical symptoms associated with late luteal phase dysphoric disorder (e.g., Parry et al., 1989). Women's responses to caffeine may also be different than the response seen with men. Specifically, the use of oral contraceptives may affect caffeine's alerting and performance-enhancing properties in women during the nighttime hours. The half-life and elimination time of caffeine is considerably increased (increases greater than 200% have been obtained) in women taking oral contraceptives (i.e., caffeine remains in the system for a longer period of time in women using oral contraceptives; e.g., Patwardhan et al., 1980). The effects of this interaction between caffeine and oral contraceptives on alertness and performance during sleep deprivation is unknown.

In addition to investigating sleep deprivation, this report examines circadian rhythms in women. Circadian rhythms are 24 hour neurobehavioral rhythms important for alertness, the sleep-wake process, immune function, reproduction, and aging (Badia, et al. 1992; Dollins, Zhdanova, Wurtman, Lynch, and Deng, 1994; Maestroni, 1993; Myers and Badia 1995; Reiter 1991a, 1991b). In humans, there is limited research investigating gender differences in circadian rhythms. Wever (1988) noted that in temporal isolation (an environment free of time cues) the body temperature rhythms of premenopausal women differed from those of both younger and older men whereas the body temperature rhythms of postmenopausal women did not.

Specifically, the period was longest in the premenopausal women. Czeisler et al. (1992) noted that older women had a larger circadian amplitude and a higher mean nocturnal temperature than older men. Relatedly, the results of several studies suggest that exogenous estrogen can affect circadian rhythms and sleep (e.g., Wilkinson et al., 1980). Whether mechanisms underlying circadian rhythms derived from data using males are similar to mechanisms derived from data using females will be explored.

In summary, research has shown that nighttime melatonin synthesis and body temperature can be controlled. Control of these rhythms allows enhancement of alertness and performance during sleep deprivation. As noted, ways to achieve this control is by exposure to bright light and by ingestion of caffeine during the nighttime melatonin period.

Additional data are now being collected to: (a) evaluate in women the effects of sleep deprivation on various psychological and physiological measures including alertness, performance, mood, and circadian rhythms (melatonin and temperature); (b) assess similarities between sleep-deprived women and sleep-deprived men; (c) test interventions with women (exposure to bright light, ingestion of caffeine) that are known to be effective with men for increasing alertness and performance during sustained wakefulness; (d) examine the effects of menstrual cycle phase (Follicular vs. Luteal) on women's responses to sleep deprivation (e) examine the effects of oral contraceptives on women's responses to sleep deprivation and on the interventions utilized to increase alertness and performance during sleep deprivation; and, compare these results to women not taking oral contraceptives; (f) determine whether underlying circadian rhythms derived of females are similar to those of males.

Hypothesis 1

As noted, melatonin is a hormone with hypnotic properties, and ingestion of melatonin during the daytime or nighttime hours results in decreased alertness, sleepiness, and decrements in performance (e.g., French et al., 1993; Hughes, Badia et al., 1994; Lieberman et al., 1984; Waldhauser et al., 1990). In addition, reduction of melatonin levels are associated with improved

performance (Badia et al. 1991; Wright. 1996). Thus, similar to our results using male subjects, it is hypothesized that suppression of melatonin during the nighttime by exposure to bright light and the ingestion of caffeine will result in increased alertness and performance in women throughout a 48-hr period of sleep deprivation. Female patterns will be compared with our data with males and similarities and differences noted.

Hypothesis 2

As discussed, increases in melatonin due to endogenous or exogenous sources results in decreases in temperature. Conversely, decreases in melatonin results in higher temperatures. Therefore, suppression of melatonin by photic stimulation and the ingestion of caffeine is hypothesized to result in higher temperature throughout a 48-hr period of sleep deprivation. As noted, male and female patterns will be compared.

Hypothesis 3

As noted, oral contraceptives increase the half-life and elimination time of caffeine (e.g., Patwardhan et al., 1980). Therefore, it is hypothesized that the ingestion of both substances (oral contraceptives and caffeine) will increase alertness and performance throughout the deprivation period relative to the ingestion of either substance alone.

Empirical Issues

While both melatonin and temperature levels change in a predictable manner across the menstrual cycle with maximal levels during premenses and minimal levels during periovulation (e.g., Rogacz et al., 1988; Webley & Leidenberger, 1986), no hypothesis concerning alertness and performance during the two phases is offered because a case for competing hypotheses can be made (i.e., in the Luteal phase, higher melatonin could result in worse performance and higher temperature could result in better performance). Therefore, this important question remains to be tested empirically.

Similarly, oral contraceptives affect both melatonin and temperature in a predictable manner--increasing both measures (e.g., Arendt, 1979; Potts & Wood, 1972; Webley &

Leidenberger, 1986), no hypothesis concerning alertness and performance in women using these drugs relative to those not using them is offered because competing hypotheses are equally tenable.

Year 2

During the second year of research, we plan on continuing our investigations using the same sleep deprivation protocol. Additional women will be tested under the 9 experimental conditions.

BODY

Subjects

Forty-three, healthy, female participants (aged 18-26 yr) who gave written informed consent were studied during 2 consecutive nights of sleep deprivation. Participants showed regular sleep-wake schedules (self reported bedtime between 2300 and 0200 hr and wake-time between 0700 and 1000 hr) and were low to moderate caffeine users (50 - 250 mg daily). Only moderate caffeine users were tested to minimize tolerance and withdrawal effects. Sleep schedules and caffeine intake were verified with logs for the week prior to study. In addition, subjects were free from nicotine and medication use (except oral contraceptives). Alcohol and caffeine use was prohibited for 24 hr prior to participation. Because of their effects on melatonin levels, nonsteroidal anti-inflammatory drugs were prohibited for 72 hr (Murphy et al. 1996). Participants kept menstrual cycle logs for at least 1 month prior to participating. All subjects obtained a physical exam at the Student Health Center as well as a pregnancy and progesterone test *one day prior to participating in the study*. The pregnancy test was used as a precautionary measure to ensure the health of the woman and fetus. No pregnant women were tested. Progesterone levels were recorded to ensure the luteal phase of their menstrual cycle.

Progesterone was assessed using serum samples. A single sample of blood (1 ml) was drawn at the Bowling Green State University Health Center by a Registered Nurse after a 12 hr fast. This sample was collected during the morning hours (0800-1000 hr) the Wednesday prior to participation. The blood sample was assessed for progesterone content by radio-immuno-assay (Roche Biomedical Laboratories, Dublin, OH). Progesterone levels exceeding 4.1 mIU/ml are representative of the luteal phase. Participants either met the 4.1 mIU/ml criterion Wednesday morning or showed signs of increasing progesterone levels that should put them in the Luteal phase during testing. Over 1000 subjects have been screened. Of the 42 subjects tested, 35 completed both nights of the study. Four subjects who received caffeine and four who received placebo, terminated participation after 1 night of sleep deprivation. The average age and weight of participants were 19.5 yr and 59.80 kg (131.84 lbs). Subjects were paid for their participation.

Experimental Groups

There are nine experimental conditions (see Table 1) addressing the hypotheses concerning exposure to bright light, caffeine ingestion, oral contraceptive use, and appropriate control groups. As noted, 42 women have been tested to date. With the exception of women in the follicular phase, subjects were randomly assigned to one of four conditions.

We have made a minor change to the experimental protocol from that originally proposed. Two bright light caffeine conditions have been added since recent results in sleep deprived males show this to be the most effective treatment for enhancing nighttime alertness and performance (Wright, 1996) To make this change we have dropped the planned group Bright Light Placebo-Follicular. This change in protocol will allow us to compare results between males

and females on the most effective treatment for enhancing alertness and performance during sleep deprivation.

Table 1.

Subjects and conditions tested as of 1 July 1996.

| | <u>Follicular Phase</u> | <u>Luteal Phase</u> | <u>Oral Contraceptive</u> |
|------------------------------|-------------------------|---------------------|---------------------------|
| Dim Light-Placebo | n = 5 | n = 5 | n = 4 |
| Bright Light-Placebo | ---- | n = 6 | n = 3 |
| Dim Light-Caffeine | ---- | n = 6 | n = 4 |
| Bright Light-Caffeine | ---- | n = 6 | n = 3 |

Note. ---- = condition not being tested.

Experimental Protocol

Testing began at 1930 hr Thursday and continued until 1000 hr Sunday. Participants slept from 2400 to 1000 hr Thursday evening. After awakening, they remained awake for the next 48 hr. A modified constant routine procedure was used (Czeisler et al 1990; Minors and Waterhouse 1985). During the daytime (0800 to 2000 hr), ambient illumination was maintained at ≤ 88 lux. One subject was assigned to each experimental room where they remained seated (nonrecumbent) in chairs throughout most of the study. Ambient temperature in the rooms was maintained at $25.6 \pm 1.7^{\circ}\text{C}$ ($78 \pm 3^{\circ}\text{F}$). Food was provided in aliquots every 3 hr. The diet was based on 3,000 cal/day (RDA + 40%; USDA, 1981) to allow for increased energy need during sleep deprivation. Each aliquot consisted of approximately 375 cal.

From 2000 to 0800 hr, subjects remained under either dim (< 88 lux) or bright ($> 5,000$ lux) illumination depending on the treatment condition. Light sources in the "bright light room" consisted of a bank of three light boxes: from Lighting Resources (Columbus, OH, USA) and Apollo Light Systems (Orem, UT, USA), placed approximately 1 m in front of the subjects. In addition, one 500 watt halogen lamp, shielded from direct illumination of the eyes, illuminated the background. During the performance testing on computers, light intensity was reduced to a minimum of 2,000 lux to reduce glare on the computer screens. In addition, subjects wore black medical scrubs and an antiglare shield was placed on the computer monitor to prevent light glare from interfering with performance testing. At all other times subjects received approximately 5,000 lux. All lux measurements were taken at eye level. Half the subjects in each lighting condition received either placebo (200 mg sugar) or 100 to 200 mg of caffeine ("Eleveine"--Alva-Amco Pharmacal Co., Chicago, IL, USA). For the first 15 subjects tested, either caffeine or a placebo was administered in a double-blind manner with water and food at 2000 and 0200 hr each night. The caffeine protocol was modified following reports by several subjects that they experienced mild stomach upset and nervousness. All subsequent subjects were given 100 mg of caffeine 4 times a night (2000 hr, 2300 hr, 0200 hr, 0500 hr) instead of 200 mg twice each night (2000 hr and 0200 hr). The total amount of caffeine ingested each night remained at 400 mg. After the change in protocol was made no further side effects were observed.

When subjects were not performing tasks, they were permitted to watch taped movies, play video games (1000 to 1800 hr only), read, do homework, play cards or converse with a member of the research staff. A member of the staff remained with the subjects at all times except during collection of EEG data.

Dependent Measures

Several neurobehavioral measures were used to examine alertness and performance during the nighttime hours. These measures were recorded in 3 hr blocks from 2000 to 0800 hr each night.

Performance Tasks. Performance batteries were composed of tasks from the Walter Reed Performance Assessment Battery, the United Triservice Performance Assessment Battery, and several tasks from the sleep laboratories of the University of Pennsylvania and Bowling Green State University (Dinges et al. 1993, 1994; Gillooly et al. 1990; Thorne 1990; Thorne et al. 1985). These tasks included, the Dual Task, the Wilkinson Four Choice Reaction Time, the Switching Task, a modified version of the Psychomotor Vigilance Task, Two-Column Addition, Continuous Recognition, Reaction Time task—Time Uncertainty Block, Digit Recall, Probed Forced Memory Recall, and the Thurstone—word generating task.

Subjects practiced performance tasks from 2000 to 2400 hr Thursday night as well as from 1100 to 1800 hr Friday day. Each subject practiced tests until asymptotic performance was obtained (i.e., less than a 10% change in performance between the last two practice trials).

Only throughput scores were analyzed except for tasks not having a throughput score. Throughput is derived from accuracy and speed data yielding a measure of correct responses per minute. The throughput measure is thus sensitive to changes in accuracy and speed performance.

Measures of Alertness. Measures of alertness included the Maintenance of Wakefulness Test (MWT; Mitler et al. 1982), Stanford Sleepiness Scale (SSS; Hodes et al. 1973), and spectral analysis of the EEG. These measures were recorded during each 3-hr block across the successive 24-hr periods. Latencies to sleep on the MWT were scored using the criteria of Rechtschaffen

and Kales (1968). Sleep onset was defined as 3 continuous epochs of any stage of sleep. For MWT and spectral data, EEG activity was acquired over 3 brain sites (Fz, Cz, Oz) referenced to linked mastoids using a Grass Model 7 Polygraph. Standard mentalis EMG, and EOG activities were also recorded to assist in sleep stage scoring. Each EEG amplifier (Grass model 7P511) was set at a sensitivity of 5 $\mu\text{V}/\text{mm}$ and used a frequency bandwidth (filter settings) of 0.3 to 100.0 Hz. A 60 Hz notch filter was used to attenuate electrical interference noise. A 50- μV sign wave signal was used for calibration. Impedances for the EEG electrodes were maintained at less than 10 Kohms. For EEG spectrals, 1 minute of eyes closed data were acquired at a rate of 200 samples per second per channel with a 12 bit Data Translations 2821 A-D board. Data were assessed for changes in amplitude by submitting the digitized EEG data to a Fast Fourier Transform (FFT) in manually selected epochs (Rhythm v. 9.0; Stellate Systems, Westmount, Canada). The EEG data were then accumulated in power ($\mu\text{V}^2/\text{Hz}$) over a frequency bandwidth of 1.5 - 30.0 Hz. in 1s bins. Artifacts were removed from data prior to analysis. Spectra of epochs with EEG artifacts (e.g., muscle artifact, amplifier blocking) were eliminated on the basis of visual inspection. If fewer than 30s of artifact free epochs were available, the spectral was omitted from further processing. The Profile of Mood States (POMS; McNair et al. 1981) was also administered in each three hour block to measure mood across the deprivation period.

Melatonin and Temperature Measurement. Melatonin content in saliva was measured on both nights of sleep deprivation. Approximately 2 ml of saliva were collected (unstimulated) into polystyrene tubes every 1 hr from 2000-1000 hr. Saliva was always gathered prior to administration of food and subjects were required to brush their teeth (without toothpaste) and rinse their mouths after every food aliquot. All samples were immediately centrifuged at 2,500

rpm for 5 min and frozen at -20 °C until assayed. Saliva melatonin levels were determined by radio-immunoassay I¹²⁵ (Alpco, LTD. Windham, NH. U.S.A) performed by the Radioimmunoassay Laboratory of Fort Rucker (Fort Rucker, AL). The average interassay coefficient of variation of the ALPCO assay is 11.75% and the intraassay coefficient of variation is 6.7-7.5%. The minimum level of detection (defined as the concentration at 2 S.D. from the counts at maximum or zero binding) was 0.3 pg/ml. Several saliva samples had to be diluted during the process of analysis. Results for these samples were suspect as the amount of melatonin measured did not correspond with the results for samples immediately prior to or after. Therefore, samples diluted were replaced with an average of the sample prior to and the sample immediately after the one in question. If more than one sample in a row was diluted, those samples were counted as missing data.

Tympanic temperature ("First Temp"--Intelligent Medical Systems, Carlsbad, CA. USA) was recorded every half hour during the evening and every hour during the daytime. A minimum of two measures that differed by no more than 0.056 °C (0.1 °F) was required for reliability at each measurement. If the two measurements were not exactly the same, the higher of the two was used.

RESULTS

Since only a portion of subjects in each treatment has been tested, statistical analyses of the data were not undertaken. However, a descriptive analyses for the data collected to date is provided. To address the questions proposed in the current report, results will be presented for performance, alertness, mood, melatonin, and body temperature measures in three sections: (A)

Effect of Caffeine and Light Treatments Collapsed Across Menstrual Phase and Oral Contraceptive Use; **(B)** Effects of Follicular and Luteal Phase and Oral Contraceptive Use on Women During Sleep Deprivation Under Dim Light Placebo Condition; and **(C)** Effect of Caffeine and Light Treatment on Women During Sleep Deprivation: Influence of Oral Contraceptive Use.

This annual report includes performance data for the Dual Task (Throughput and Control Losses), the Wilkinson Four Choice Reaction Time (Throughput), and the Switching Task (Mannequin and Math Throughput). The final report will also include results for the following performance measures: a modified version of the Psychomotor Vigilance Task, Two-Column Addition, Continuous Recognition, Reaction Time task—Time Uncertainty Block, Digit Recall, Probed Forced Memory Recall, and the Thurstone—word generating task. Alertness data for the MWT and SSS will be presented in this annual report. Objective alertness will also be measured using power spectral analysis of EEG activity and will be presented in the final report. Mood results for the POMS and PANAS are presented in this report. Hourly melatonin and temperature measures are also presented in the current report. Additional results for a circadian analysis of the body temperature data will be presented in the final report (Brown and Czeisler, 1992). Circadian temperature amplitude, phase and mesor values will be examined using data from 1100 to 1000 hr each day. The circadian analysis will not be performed on the melatonin data since melatonin samples are not taken during the daytime hours.

(A). Effect of Caffeine and Light Treatments Collapsed Across Menstrual Phase and Oral Contraceptive Use.

These results describe the effects of sleep deprivation on women regardless of menstrual phase and oral contraceptive use. The effectiveness of caffeine and bright light treatments for increasing alertness and performance and for modifying the circadian rhythms of melatonin and temperature during sustained wakefulness are described for the following conditions:

| | | | |
|-------------------|--------------------|----------------------|-----------------------|
| Dim Light Placebo | Dim Light Caffeine | Bright Light Placebo | Bright Light Caffeine |
|-------------------|--------------------|----------------------|-----------------------|

Performance Measures

The effect of bright light and caffeine on performance during sleep deprivation will be examined first. In general, performance was worst in the Dim Light-Placebo conditions. Bright Light and Caffeine conditions maintained higher levels of nighttime performance during sleep deprivation. Results are presented for the Dual Task, the Wilkinson Four Choice Reaction Time, and the Switching Task.

Dual Task—Throughput, Dual Task—Control Losses, and Wilkinson Four Choice Reaction Time. Figures 1A-1C present data for both Throughput and Control Loss measures of the Dual Task and for the Throughput measure of the Wilkinson task. As seen, nighttime performance was better for caffeine and bright light conditions versus the Dim Light-Placebo condition: especially during the early morning hours.

Switching Task—Mannequin Throughput and Switching Task—Math Throughput. In general, Switching Task Math and Mannequin Throughput performance were better for caffeine conditions compared to placebo conditions (Figures 2A-2B). However, Bright Light-Placebo did show some performance enhancement during the early morning hours (between 0200 and 0800 hr).

Alertness

The effect of bright light and caffeine on objective and subjective measures of alertness during sleep deprivation will be examined next. In general, alertness was worst in the Dim Light-Placebo conditions. Bright Light and Caffeine conditions maintained higher levels of nighttime alertness during sleep deprivation.

Maintenance of Wakefulness Test (MWT)

Dim Light-Caffeine (Nights 1 and 2) and Bright Light-Placebo (Night 2) appear to have some enhancing effect on alertness; especially during the early morning hours between 0200 and 0800 hr (Figure 3). The most marked effects on objective alertness are observed in the combined Bright Light-Caffeine condition (Figure 3). Alertness is highest in the combined treatment condition, especially on Night 2 of sleep deprivation. Latencies to sleep are shorter on Night 2 compared to Night 1 for all groups.

Stanford Sleepiness Scale (SSS)

Figure 4 provides SSS data every 3 hr for each treatment condition on both nights. As seen, sleepiness increases with sleep deprivation. The caffeine and light treatments show less subjective sleepiness than the Dim Light-Placebo condition on Night 1, whereas on Night 2, only

the bright light conditions show less sleepiness than the Dim Light-Placebo condition during the early morning hours (Figure 4).

Mood

Profile of Mood States (POMS)

The scores of all six sub-scales of the POMS changed as a result of sleep deprivation (Figure 5). Anger-Hostility, Depression-Dejection, Confusion-Bewilderment, Tension-Anxiety, and Fatigue-Inertia, increased whereas Vigor-Activity decreased (Figure 5). In general, little systematic effect of the treatments on mood are seen. On Night 2 however, women in the Bright Light-Caffeine Condition show higher Anger-Hostility, Depression-Dejection, and Tension-Anxiety scores relative to the other conditions (Figure 5).

Positive Affective Negative Affective Scale (PANAS)

Positive affect decreased while negative affect increased slightly as a result of sleep deprivation (Figures 6A-6B). The combined treatment of Bright Light-Caffeine showed the highest scores of positive mood across both nights of sleep deprivation. Positive affect scores are similar in the Dim Light-Caffeine, Bright Light-Placebo and Dim Light-Placebo conditions; with the exception of Bright Light-Placebo on Night 2 which showed less positive affect than all conditions (Figure 6A). Little effect of the treatments on negative affect are observed on Night 1, but on Night 2, Bright Light-Placebo showed the highest negative affect (Figure 6B).

Melatonin and Body Temperature

Melatonin

Bright Light treatments reduced melatonin levels relative to the Dim Light-Placebo condition (Figures 7A-7B). Caffeine alone appears to reduce melatonin levels the beginning of

Night 1 (Figure 7A). On Night 2, caffeine appears to have little affect on melatonin levels (Figure 7B).

Body Temperature

In general, the Caffeine and Bright Light treatments attenuated the nighttime drop in body temperature compared to Dim Light-Placebo (Figure 8A-8B). On Night 1, the combined treatment of Caffeine and Bright Light produced the most marked effect on temperature (Figure 8A). On Night 2, caffeine alone has less of an effect on temperature levels (Figure 8B).

(B). Effects of Follicular and Luteal Phase and Oral Contraceptive Use on Women During Sleep Deprivation Under Dim Light Placebo Condition.

These results evaluate the effects of menstrual cycle phase (Follicular vs. Luteal) and Oral Contraceptive use on women's responses to sleep deprivation and on circadian rhythms. Data are compared for women tested under Dim Light Placebo conditions. Note that these results are tentative since the experimental conditions are only partially completed. Data are described for the following conditions:

| | | |
|----------------------------------|------------------------------|--|
| Dim Light Placebo- Follicular | Dim Light Placebo- Luteal | Dim Light Placebo- Oral Contraceptive |
|----------------------------------|------------------------------|--|

Performance Measures

In general, performance was best for women in the Luteal Phase of their menstrual cycle. Little difference was observed between women taking Oral Contraceptives and women in the Follicular Phase of their cycle.

Dual Task—Throughput, Dual Task—Control Losses, and Wilkinson Four Choice Reaction Time.

Throughput and Control Loss measures of the Dual Task show the best performance for women in the Luteal Phase of the menstrual cycle compared to women in the Follicular Phase or in those taking Oral Contraceptives (Figure 9A-9B). Women in the Follicular Phase perform the worst on the Wilkinson task. (Figure 9C).

Switching Task—Mannequin Throughput and Switching Task—Math Throughput.

In general, Throughput performance on the Switching Task appears slightly better for women in the Luteal Phase of the menstrual cycle compared to women in the Follicular Phase and in those taking Oral Contraceptives (Figure 10A-10B).

Alertness

In general, there appears little effect of menstrual cycle phase and oral contraceptive use on objective and subjective measures of alertness during sleep deprivation.

Maintenance of Wakefulness Test (MWT)

The effect of menstrual cycle phase (Luteal vs. Follicular) and Oral Contraceptive use on the MWT appears minimal (Figure 11).

Stanford Sleepiness Scale (SSS)

The effect of menstrual cycle phase (Luteal vs. Follicular) and Oral Contraceptive use on subjective sleepiness appears minimal (Figure 12).

Mood

In general, there appears little effect of menstrual cycle phase and oral contraceptive use on mood during sleep deprivation.

Profile of Mood States (POMS)

The effect of menstrual cycle phase (Luteal vs. Follicular) on mood as measured by the POMS appears minimal. However, mood scores for Tension-Anxiety and Confusion-Bewilderment are highest in the Oral Contraceptive group on Night 2 between 2300 and 0800 hr (Figure 13).

Positive Affective Negative Affective Scale (PANAS)

The effect of menstrual cycle phase (Luteal vs. Follicular) and Oral Contraceptive use on positive and negative affect appears minimal (Figure 14A-14B).

Melatonin and Body Temperature

Melatonin

No description is provided for melatonin data since to date only 2 subjects for each condition have been analyzed. Graphs are presented for the data analyzed (Figures 15A-15B).

Body Temperature

Body temperature levels are highest in the Oral Contraceptive group on both nights of sleep deprivation compared to women not taking oral contraceptives. Women in the Follicular Phase of the menstrual cycle show the lowest temperature levels on Night 1, whereas on Night 2, little difference is observed between Follicular and Luteal Phases (Figure 16A-16B).

(C). Effect of Caffeine and Light Treatment on Women During Sleep Deprivation:

Influence of Oral Contraceptive Use.

These results examine whether oral contraceptive use influences the effectiveness of the caffeine and bright light treatments to modify alertness, performance, and circadian rhythms in

sleep deprived women. Note that the results are tentative since the experimental conditions are only partially completed. Data are described for the following conditions:

| | | | |
|---|--|--|---|
| Dim Light Placebo - Luteal | Dim Light Caffeine - Luteal | Bright Light Placebo - Luteal | Bright Light Caffeine - Luteal |
| Dim Light Placebo - Oral Contraceptive | Dim Light Caffeine - Oral Contraceptive | Bright Light Placebo - Oral Contraceptive | Bright Light Caffeine - Oral Contraceptive |

Performance Measures

In general, performance was worst in the placebo conditions. Caffeine conditions maintained higher levels of nighttime performance during sleep deprivation for both women taking and not taking oral contraceptives. Performance in the Bright Light Placebo condition appears to be worse for women taking Oral Contraceptives than in women not taking them.

Dual Task—Throughput, Dual Task—Control Losses, and Wilkinson Four Choice Reaction Time.

Dim Light-Caffeine and Bright Light Caffeine treatment generally produce improved performance in women taking and not taking oral contraceptives (Figure 17A-17C). For the Dim Light-Caffeine condition, performance on the Dual Task – Throughput measure appears better in women taking Oral Contraceptives than in those not taking the drug; especially during the early morning hours on Night 2 (Figure 17A; see also Appendix Figures A17A1-A2, and B17(a)A1-A4). Women taking Oral Contraceptives appear to benefit less from Bright Light-Placebo

treatment compared to women not using oral contraceptives (Figure 17A-17C; see also Appendix Figures A17A1-A2, A17B1-B2, A17C1-C2, B17(a)A1-A4, B17(b)B1-B4, and B17(c)C1-C4).

Switching Task—Mannequin Throughput and Switching Task—Math Throughput.

In general, Dim Light-Caffeine and Bright Light-Caffeine treatments enhance performance compared to the Dim Light-Placebo condition for women taking and not taking Oral Contraceptives (Figures 18A-18B; see also Appendix Figures A18A1-A2, A18B1-B2, B18(a)A1-A4, and B18(b)B1-B4). In addition, women taking Oral Contraceptives appear to do better than those not taking oral contraceptives under Dim Light-Caffeine treatment (Figures 18A-18B; see also Appendix Figures A18A1-A2, A18B1-B2, B18(a)A2, and B18(b)B2). Women taking and not taking oral contraceptives appear to perform equally well under Bright Light-Caffeine treatment. Compared to the Dim Light-Placebo condition, the Bright Light-Placebo condition produced better performance for the Switching Task Mannequin and Math Throughput tasks for women not taking oral contraceptives. Women taking Oral Contraceptives appear to perform worse in the Bright Light Placebo condition than in the Dim Light-Placebo condition (Figures 18A-18B; see also Appendix Figures A18A1-A2, A18B1-B2, B18(a)A3, and B18(b)B3).

Alertness

The effect of oral contraceptive use on women's response to the alerting effect of bright light and caffeine treatment during sleep deprivation will be examined next. In general, alertness was worst in the Dim Light-Placebo condition. Bright light and caffeine conditions maintained higher levels of nighttime alertness during sleep deprivation.

Maintenance of Wakefulness Test (MWT)

Bright Light-Caffeine treatment maintains high levels of alertness on the MWT for women taking and not taking oral contraceptives (Figure 19; see also Appendix Figures A19A1-A2 and B19A1-A4). For women not taking oral contraceptives, Bright Light-Placebo treatment does not improve alertness compared to the Dim Light-Placebo condition. On the other hand, Bright Light-Placebo appears to have some improvement on alertness in women taking Oral Contraceptives on Night 2 of sleep deprivation. Oppositely, Dim Light-Caffeine appears to have some alerting effect compared to Dim Light-Placebo for women not taking oral contraceptives than in women taking them.

Stanford Sleepiness Scale (SSS)

Neither bright light, caffeine or use of Oral Contraceptives appear to affect subjective sleepiness (Figure 20; see also Appendix Figures A20A1-A2 and B20A1-A4).

Mood

The effect of oral contraceptive use on women's mood response to bright light and caffeine treatment during sleep deprivation will be examined next. In general, the use of Oral Contraceptives show some interaction with the caffeine and light treatments for effects on mood during sleep deprivation.

Profile of Mood States (POMS)

The use of Oral Contraceptives appears to have some effect on mood when tested under the caffeine and light treatments. Specifically, for the Dim Light-Caffeine condition less Fatigue-Inertia (Night 2) and Confusion-Bewilderment are observed in women taking Oral

Contraceptives than in women not taking them (Figure 21D & 21E; see also Appendix Figures A21(a)D1-D2, A21(b)E1-E2, B21(b)D1 and B21(b)E1). In the Bright Light-Placebo condition, women taking Oral Contraceptives show less Tension-Anxiety, Depression-Dejection, and Confusion-Bewilderment especially on Night 2 compared to women not taking oral contraceptives (Figure 21B, 21C, & 21E; see also Appendix Figures A21(a)B1-B2, A21(a)C1-C2, A21(b)E1-E2, B21(c)B1, B21(c)C1 and B21(c)E1). For the Bright Light-Caffeine condition, women taking Oral Contraceptives show lower Anger-Hostility, Tension-Anxiety (Night 1), Depression-Dejection, Fatigue-Inertia (Night 1), and Confusion-Bewilderment (Night 1), and higher Vigor-Activity (Night 1) than in those not taking them (Figure 21A-F; see also Appendix Figures A21(a)A1-C2, A21(b)D1-F2, B21(d)A1-F1).

Positive Affective Negative Affective Scale (PANAS)

The use of Oral Contraceptives seems to interact with the bright light and caffeine treatments for positive affect. In general, less positive affect is observed in women taking Oral Contraceptives than in women not taking them when tested under the caffeine and bright light treatments (Figures 22A; see also Appendix Figures A22A1-A2, B22(a)A1-A4). Negative affect in the caffeine conditions is similar for those taking and not taking oral contraceptives (Figure 22B see also Appendix Figures A22B1-B2, B22(b)B1-B4). For women in the Bright Light-Placebo condition, negative affect is highest in women not taking oral contraceptives.

Melatonin and Body Temperature

The effect of oral contraceptive use on women's physiological response to bright light and caffeine treatment during sleep deprivation will be examined next.

Melatonin

No description is provided for melatonin data since to date only 2 subjects for each condition have been analyzed. Graphs are presented for the data analyzed (Figure 23A-23B; see also Appendix Figures A23A1-B2 and B23A1-A8).

Body Temperature

The ability of the Dim Light-Caffeine and the Bright Light-Caffeine treatments to maintain high nighttime temperature levels appears to be enhanced in women taking Oral Contraceptives compared to women not taking them (Figure 24A-24B; see also Appendix Figures A24A1-B2 and B24A1-A8). Conversely, the Bright Light-Placebo treatment is equally effective in maintaining high temperature levels in women taking and not taking oral contraceptives.

PRELIMINARY CONCLUSIONS

Preliminary results are promising, however the results are tentative since the experimental conditions are only partially completed. The effects of sleep deprivation on various psychological and physiological measures including alertness, performance, mood, and circadian rhythms (melatonin and temperature) in women appear to be similar to those found with men tested in our laboratory over the past 5 years.

(A). Effect of Caffeine and Light Treatments Collapsed Across Menstrual Phase and Oral Contraceptive Use.

Interventions (i.e., exposure to bright light and ingestion of caffeine) that are known to be effective with men for increasing alertness and performance during sustained wakefulness also appear effective in women.

(B). Effects of Follicular and Luteal Phase and Oral Contraceptive Use on Women During Sleep Deprivation Under Dim Light Placebo Condition.

Women in the Luteal Phase appear to perform better than women in either the Follicular Phase or women using Oral Contraceptives. Menstrual cycle phase and Oral Contraceptive use appears to have little effect on alertness and mood during sleep deprivation. As expected, body temperature levels appear higher in women using Oral Contraceptives than in women not using them. There is not enough data to determine whether Menstrual cycle phase and Oral Contraceptive use affects melatonin levels.

(C). Effect of Caffeine and Light Treatment on Women During Sleep Deprivation: Influence of Oral Contraceptive Use.

Oral contraceptive use appears to reduce the ability of the Bright Light-Placebo condition to enhance performance. However, performance for women tested in the Dim Light-Caffeine condition, appears to be enhanced in those taking Oral Contraceptives than in those not taking them. Women taking and not taking oral contraceptives appear to perform equally well under Bright Light Caffeine treatment. Alertness level shows little effect of an interaction

between Oral Contraceptive use and the caffeine and bright light treatments. Negative mood appears to be improved in the caffeine and bright light treatment conditions for women taking Oral Contraceptives compared to those not taking contraceptives. Positive affect however, for those tested in the caffeine and bright light treatments, appears to be worse for Oral Contraceptive users than non users. Body temperature levels for women tested in the caffeine conditions are higher in those taking oral contraceptives than in women not taking contraceptives. Bright light alone appears to have little interaction with oral contraceptives for an effect on temperature. There is not enough data to determine whether Oral Contraceptive use affects the ability of the caffeine and bright light treatments to reduce melatonin levels.

General Summary

In sum, the effects of sleep deprivation on alertness, performance, mood, melatonin, and body temperature in women appear similar to previous findings with males. Caffeine and bright light treatments, previously found to be effective in males, appear to be effective in women. There appear to be some affect of menstrual cycle phase and oral contraceptive use on women during sleep deprivation, however more subjects need to be tested to see whether these trends continue.

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FIGURE CAPTIONS

General Figure Legend

DLP = Dim Light Placebo

DLC = Dim Light Caffeine

BLP = Bright Light Placebo

BLC = Bright Light Caffeine

DLP-FOL = Dim Light Placebo-Follicular Phase

DLP-LUT = Dim Light Placebo-Luteal Phase

DLP-OC = Dim Light Placebo-Oral Contraceptive

DLC-LUT = Dim Light Caffeine-Luteal Phase

DLC-OC = Dim Light Caffeine-Oral Contraceptive

BLP-LUT = Bright Light Placebo-Luteal Phase

BLP-OC = Bright Light Caffeine-Oral Contraceptive

BLC-LUT = Bright Light Placebo-Luteal Phase

BLC-OC = Bright Light Caffeine-Oral Contraceptive

For Performance Tasks:

P = last practice trial prior to treatment onset Friday and Saturday (1700 hr)

- 1) the higher the Throughput scores = the better the performance
- 2) the lower the Control Losses = the better the performance

For Alertness Tests:

- 1) the longer the Latency to Sleep on the MWT = the more alert
- 2) the higher the Score on the SSS = the more sleepy

(A) Effect of Caffeine and Light Treatments Collapsed Across Menstrual Phase and Oral Contraceptive Use.

Graphs showing the effects of sleep deprivation on women regardless of menstrual phase and oral contraceptive use.

Figure Legend

DLP = Dim Light Placebo

DLC = Dim Light Caffeine

BLP = Bright Light Placebo

BLC = Bright Light Caffeine

For Performance Tasks:

P = last practice trial prior to treatment onset Friday and Saturday (1700 hr)

- 1) the higher the Throughput scores = the better the performance,
- 2) the lower the Control Losses = the better the performance.

For Alertness Tests:

- 1) the longer the Latency to Sleep on the MWT = the more alert
- 2) the higher the Score on the SSS = the more sleepy

Figure 1. Performance on the **A)** Dual Task - Throughput, **B)** Dual Task - Control Losses, and **C)** Wilkinson Four Choice Reaction Time - Throughput.

Figure 2. Performance on the **A)** Switching Task - Mannequin Throughput and **B)** Switching Task - Math Throughput.

Figure 3. Latency to sleep on the Maintenance of Wakefulness Test during sleep deprivation.

Figure 4. Subjective sleepiness on the Stanford Sleepiness Scale.

Figure 5. Mood for the Profile of Mood States 6-subscales.

Figure 6. **A)** Positive and **B)** Negative Affect for the Positive Affect Negative Affect Scale.

Figure 7. Hourly salivary melatonin levels from 2000 to 1000 hr **A)** Night 1. **B)** Night 2.

Figure 8. Tympanic temperature every 30 min from 2000 to 1000 hr **A)** Night 1. **B)** Night 2.

(B) Effects of Follicular and Luteal Phase and Oral Contraceptive Use on Women During Sleep Deprivation Under Dim Light Placebo Condition.

Graphs showing the effects of menstrual cycle phase (Follicular vs. Luteal) and Oral Contraceptive use on women's responses to sleep deprivation and on circadian rhythms. Data are presented for women tested under Dim Light Placebo conditions.

Figure Legend

DLP-FOL = Dim Light Placebo-Follicular Phase
DLP-LUT = Dim Light Placebo-Luteal Phase
DLP-OC = Dim Light Placebo-Oral Contraceptive

For Performance Tasks:

P = last practice trial prior to treatment onset Friday and Saturday (1700 hr)

- 1) the higher the Throughput scores = the better the performance
- 2) the lower the Control Losses = the better the performance

For Alertness Tests:

- 1) the longer the Latency to Sleep on the MWT = the more alert
- 2) the higher the Score on the SSS = the more sleepy

Figure 9. Performance on the **A)** Dual Task - Throughput, **B)** Dual Task - Control Losses, and **C)** Wilkinson Four Choice Reaction Time Task - Throughput.

Figure 10. Performance on the **A)** Switching Task - Mannequin Throughput and **B)** Switching Task - Math Throughput.

Figure 11. Latency to sleep on the Maintenance of Wakefulness Test.

Figure 12. Subjective sleepiness on the Stanford Sleepiness Scale.

Figure 13. Mood for the Profile of Mood States 6-subscales.

Figure 14. **A)** Positive and **B)** Negative Affect for the Positive Affect Negative Affect Scale.

Figure 15. Hourly salivary melatonin levels from 2000 to 1000 hr **A)** Night 1, **B)** Night 2.

Figure 16. Tympanic temperature every 30 min from 2000 to 1000 hr **A)** Night 1, **B)** Night 2.

(C) Effect of Caffeine and Light Treatment on Women During Sleep Deprivation:**Influence of Oral Contraceptive Use.**

Graphs showing whether oral contraceptive use influences the effectiveness of the caffeine and bright light treatments to modify alertness, performance, and circadian rhythms in sleep deprived women.

Figure Legend

| | |
|---------|--|
| DLP-FOL | = Dim Light Placebo-Follicular Phase; |
| DLP-LUT | = Dim Light Placebo-Luteal Phase |
| DLP-OC | = Dim Light Placebo-Oral Contraceptive |
| DLC-LUT | = Dim Light Caffeine-Luteal Phase |
| DLC-OC | = Dim Light Caffeine-Oral Contraceptive |
| BLP-LUT | = Bright Light Placebo-Luteal Phase |
| BLP-OC | = Bright Light Caffeine-Oral Contraceptive |
| BLC-LUT | = Bright Light Placebo-Luteal Phase |
| BLC-OC | = Bright Light Caffeine-Oral Contraceptive |

For Performance Tasks:

P = last practice trial prior to treatment onset Friday and Saturday (1700 hr)

- 1) the higher the Throughput scores = the better the performance
- 2) the lower the Control Losses = the better the performance

For Alertness Tests:

- 1) the longer the Latency to Sleep on the MWT = the more alert
- 2) the higher the Score on the SSS = the more sleepy

Figure 17. Performance on the **A)** Dual Task - Throughput, **B)** Dual Task - Control Losses, and **C)** Wilkinson Four Choice Reaction Time Task - Throughput.

Figure 18. Performance on the **A)** Switching Task - Mannequin Throughput and **B)** Switching Task - Math Throughput.

Figure 19. Latency to sleep on the Maintenance of Wakefulness Test.

Figure 20. Subjective sleepiness on the Stanford Sleepiness Scale.

Figure 21. Mood for the Profile of Mood States 6-subscales.

Figure 22. **A)** Positive and **B)** Negative Affect for the Positive Affect Negative Affect Scale.

Figure 23. Hourly salivary melatonin levels from 2000 to 1000 hr **A)** Night 1, **B)** Night 2.

Figure 24. Tympanic temperature every 30 min from 2000 to 1000 hr **A)** Night 1, **B)** Night 2.

APPENDIX A

Graphs comparing caffeine and light treatments in women taking and not taking oral contraceptives. These graphs show the pattern of findings for the caffeine and light treatments for women in the Luteal Phase and for women taking Oral Contraceptives.

Figure A17. Performance on the **A1)** Dual Task - Throughput for women in the Luteal Phase, **A2)** Dual Task - Throughput for women taking Oral Contraceptives; **B1)** Dual Task - Control Losses for women in the Luteal Phase, **B2)** Dual Task - Control Losses for women taking Oral Contraceptives, and **C1)** Wilkinson Four Choice Reaction Time Task - Throughput for women in the Luteal Phase, **C2)** Wilkinson Four Choice Reaction Time Task - Throughput for women taking Oral Contraceptives.

Figure A18. Performance on the **A1)** Switching Task - Mannequin Throughput for women in the Luteal Phase, **A2)** Switching Task - Mannequin Throughput for women taking Oral Contraceptives, and **B1)** Switching Task - Math Throughput for women in the Luteal Phase, **B2)** Switching Task - Math Throughput for women taking Oral Contraceptives.

Figure A19. Latency to sleep on the Maintenance of Wakefulness Test **A1)** for women in the Luteal Phase, **A2)** for women taking Oral Contraceptives.

Figure A20. Subjective sleepiness on the Stanford Sleepiness Scale **A1)** for women in the Luteal Phase, **A2)** for women taking Oral Contraceptives.

Figure A21(a). Mood for the Profile of Mood States **A1)** Anger-Hostility for women in the Luteal Phase, **A2)** Anger-Hostility for women taking Oral Contraceptives, **B1)** Tension-Anxiety for women in the Luteal Phase, **B2)** Tension-Anxiety for women taking Oral Contraceptives, and

C1) Depression-Dejection for women in the Luteal Phase. **C2)** Depression-Dejection for women taking Oral Contraceptives.

Figure A21(b). Mood for the Profile of Mood States **D1)** Fatigue-Inertia for women in the Luteal Phase. **D2)** Fatigue-Inertia for women taking Oral Contraceptives. **E1)** Confusion Bewilderment for women in the Luteal Phase. **E2)** Confusion Bewilderment for women taking Oral Contraceptives and **F1)** Vigor-Activity for women in the Luteal Phase. **F2)** Vigor-Activity for women taking Oral Contraceptives.

Figure A22. Positive Affect Negative Affect Scale: **A1)** Positive Affect for women in the Luteal Phase. **A2)** Positive Affect for women taking Oral Contraceptives, and **B1)** Negative Affect for women in the Luteal Phase, **B2)** Negative Affect for women taking Oral Contraceptives.

Figure A23. Hourly salivary melatonin levels from 2000 to 1000 h: **A1)** Night 1 data for women in the Luteal Phase, **A2)** Night 1 data for women taking Oral Contraceptives, **B1)** Night 2 data for women in the Luteal Phase, and **B2)** Night 2 data for women taking Oral Contraceptives.

Figure A24. Tympanic temperature every 30 min from 2000 to 1000 hr **A1)** Night 1 data for women in the Luteal Phase. **A2)** Night 1 data for women taking Oral Contraceptives. **B1)** Night 2 data for women in the Luteal Phase, and **B2)** Night 2 data for women taking Oral Contraceptives.

APPENDIX B

Graphs comparing women in the Follicular Phase, the Luteal Phase and women taking Oral Contraceptives. These graphs show women's responses to each caffeine and light treatment and how these responses are effected by the use of oral contraceptives.

Figure B17(a). Performance on the Dual Task - Throughput for women in the **A1)** DLP condition, **A2)** DLC condition, **A3)** BLP condition, **A4)** BLC condition.

Figure B17(b). Performance on the Dual Task - Control Losses for women in the **B1)** DLP condition, **B2)** DLC condition, **B3)** BLP condition, **B4)** BLC condition.

Figure B17(b). Performance on the Wilkinson Four Choice Reaction Time Task - Throughput for women in the **C1)** DLP condition, **C2)** DLC condition, **C3)** BLP condition, **C4)** BLC condition.

Figure B18(a). Performance on the Switching Task - Mannequin Throughput for women in the **A1)** DLP condition, **A2)** DLC condition, **A3)** BLP condition, **A4)** BLC condition.

Figure B18(b). Performance on the Switching Task - Math Throughput for women in the **B1)** DLP condition, **B2)** DLC condition, **B3)** BLP condition, **B4)** BLC condition.

Figure B19. Latency to sleep on the Maintenance of Wakefulness Test for women in the **A1)** DLP condition, **A2)** DLC condition, **A3)** BLP condition, **A4)** BLC condition.

Figure B20. Subjective sleepiness on the Stanford Sleepiness Scale for women in the **B1)** DLP condition, **B2)** DLC condition, **B3)** BLP condition, **B4)** BLC condition.

Figure B21(a). Mood for the Profile of Mood States for women in the DLP condition **A)** Anger-Hostility, **B)** Tension-Anxiety, **C)** Depression-Dejection, **D)** Fatigue-Inertia, **E)** Confusion Bewilderment, and **F)** Vigor-Activity.

Figure B21(b). Mood for the Profile of Mood States for women in the DLC condition **A)** Anger-Hostility, **B)** Tension-Anxiety, **C)** Depression-Dejection, **D)** Fatigue-Inertia, **E)** Confusion Bewilderment, and **F)** Vigor-Activity.

Figure B21(c). Mood for the Profile of Mood States for women in the BLP condition **A)** Anger-Hostility, **B)** Tension-Anxiety, **C)** Depression-Dejection, **D)** Fatigue-Inertia, **E)** Confusion Bewilderment, and **F)** Vigor-Activity.

Figure B21(d). Mood for the Profile of Mood States for women in the BLC condition **A)** Anger-Hostility, **B)** Tension-Anxiety, **C)** Depression-Dejection, **D)** Fatigue-Inertia, **E)** Confusion Bewilderment, and **F)** Vigor-Activity.

Figure B22(a). Positive affect on the Positive Affect Negative Affect Scale for women in the **A1)** DLP condition, **A2)** DLC condition, **A3)** BLP condition, **A4)** BLC condition.

Figure B22(b). Negative affect on the Positive Affect Negative Affect Scale for women in the **B1)** DLP condition, **B2)** DLC condition, **B3)** BLP condition, **B4)** BLC condition.

Figure B23. Hourly salivary melatonin levels from 2000 to 1000 hr in the **A1)** DLP condition Night 1, **A2)** DLP condition Night 2, **A3)** DLC condition Night 1, **A4)** DLC condition Night 2, **A5)** BLP condition Night 1, **A6)** BLP condition Night 2, **A7)** BLC condition Night 1, **A8)** BLC condition Night 2.

Figure B24. Tympanic temperature every 30 min from 2000 to 1000 hr in the **A1)** DLP condition Night 1, **A2)** DLP condition Night 2, **A3)** DLC condition Night 1, **A4)** DLC condition Night 2.

A5) BLP condition Night 1, **A6)** BLP condition Night 2. **A7)** BLC condition Night 1. **A8)** BLC condition Night 2.

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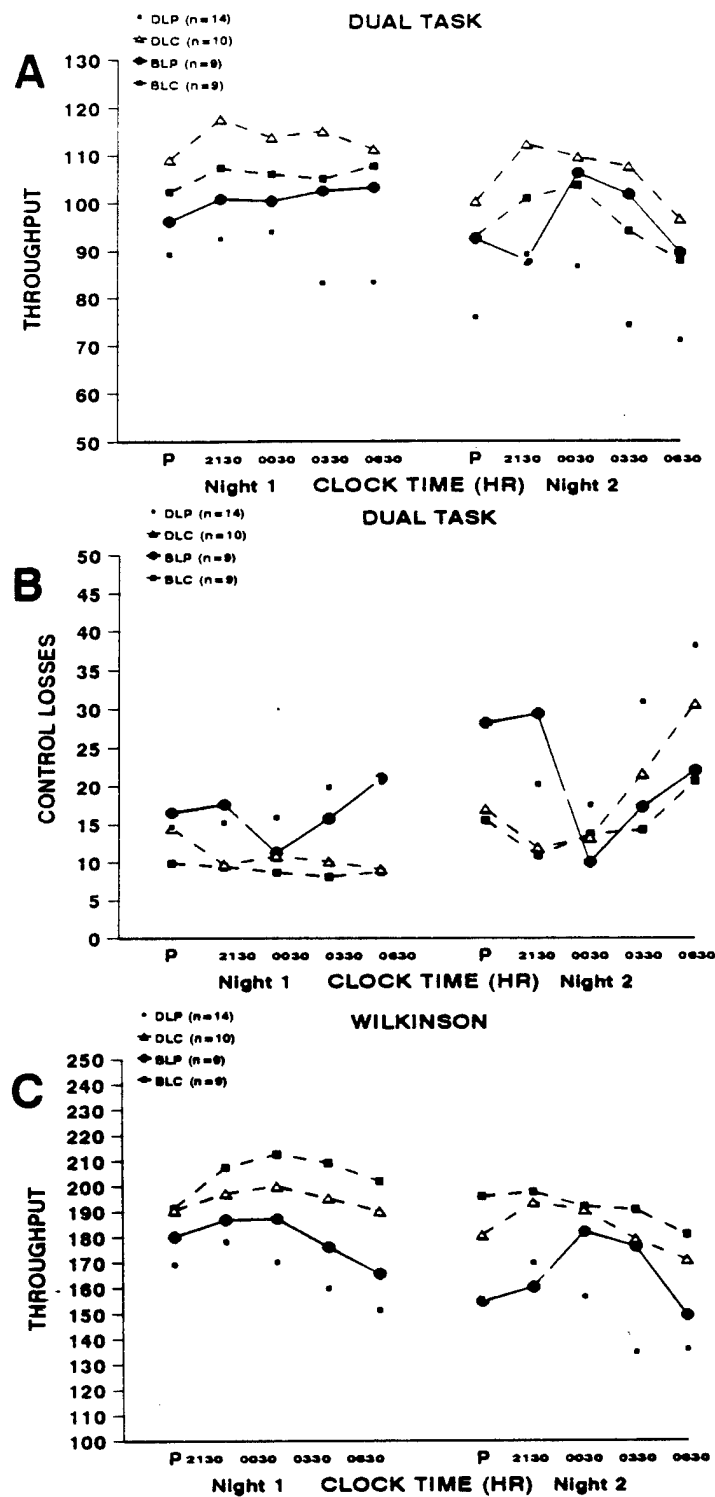


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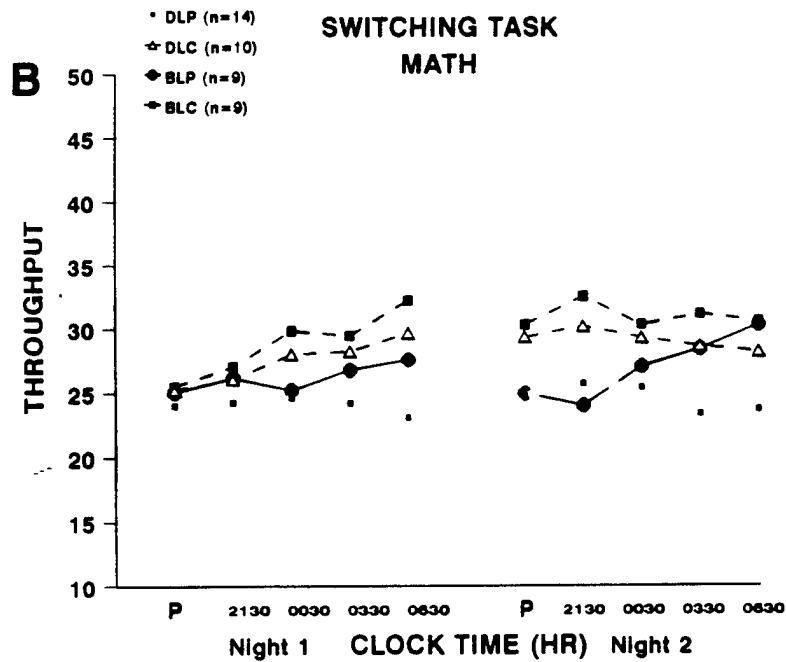
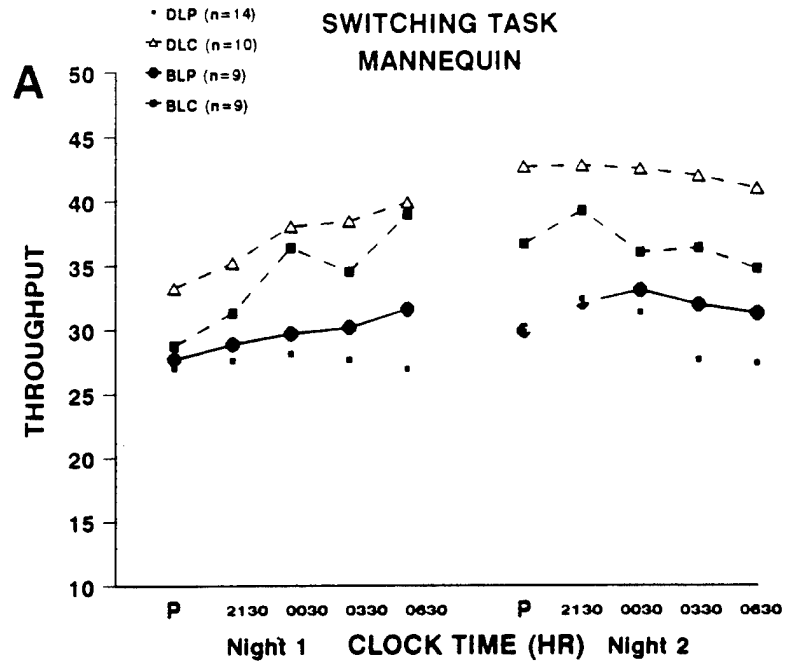


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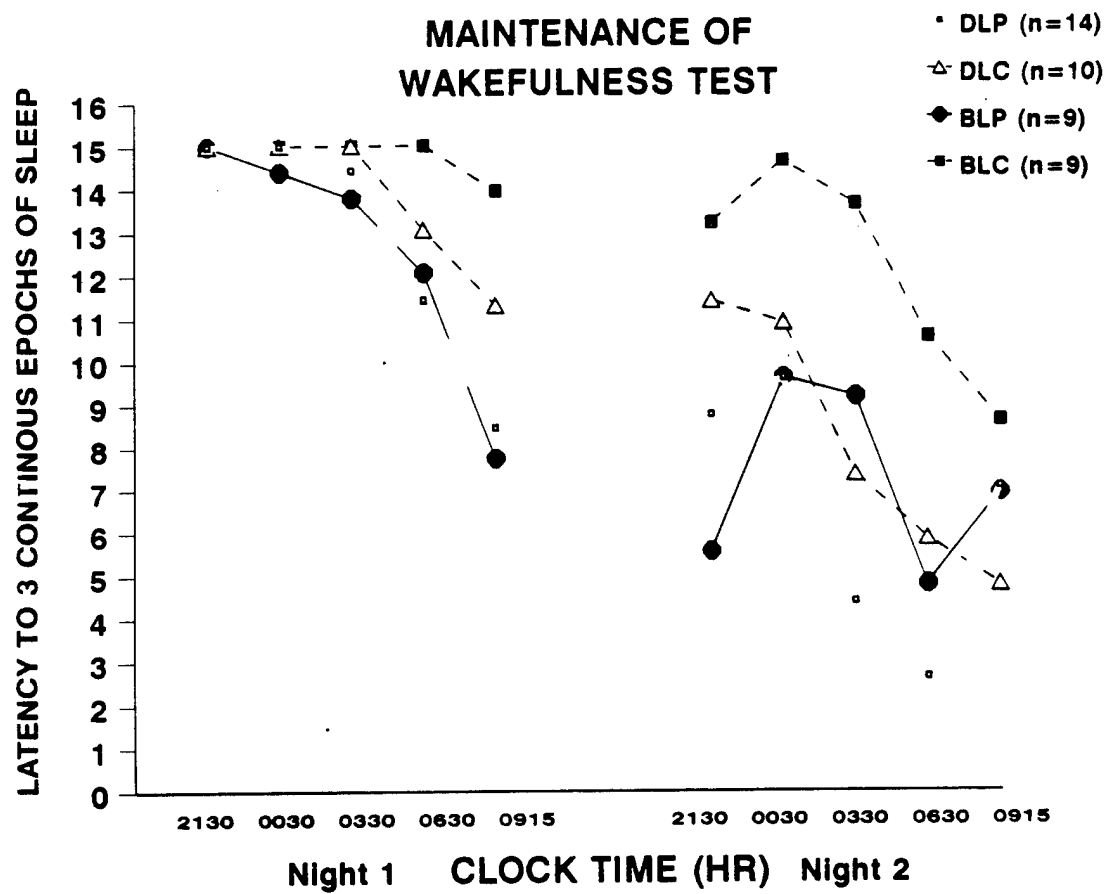
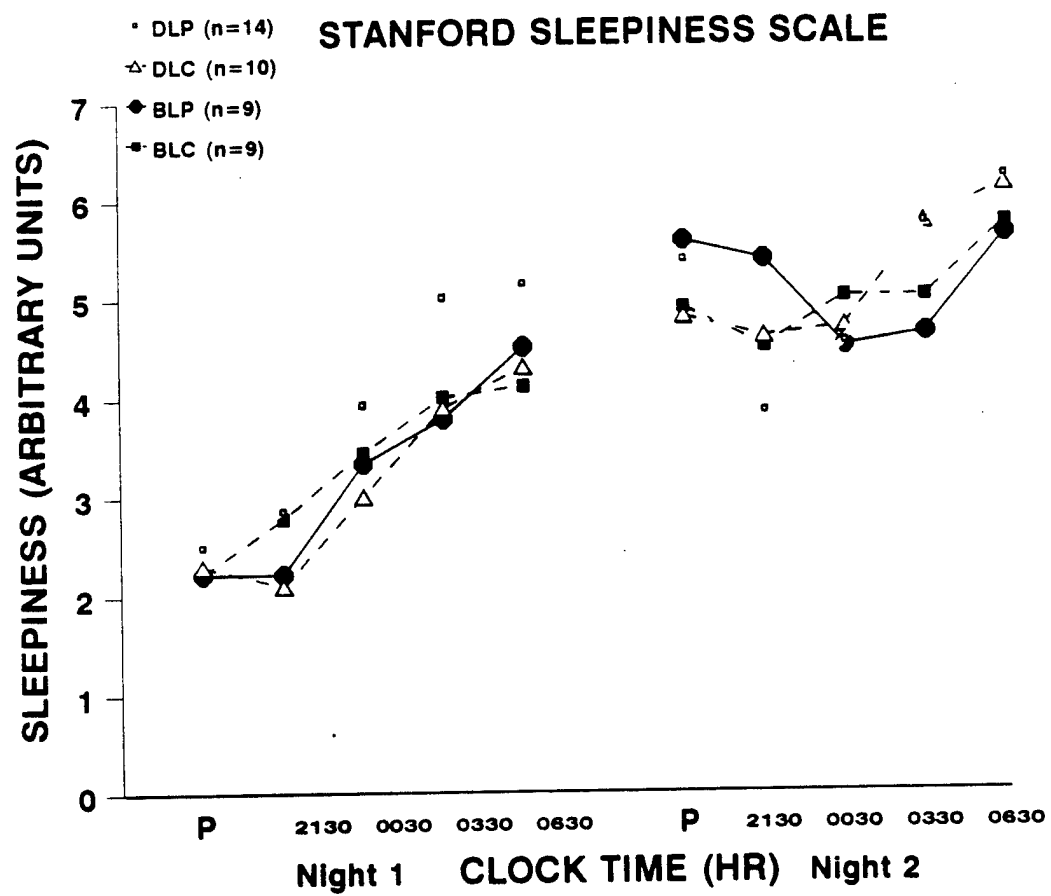


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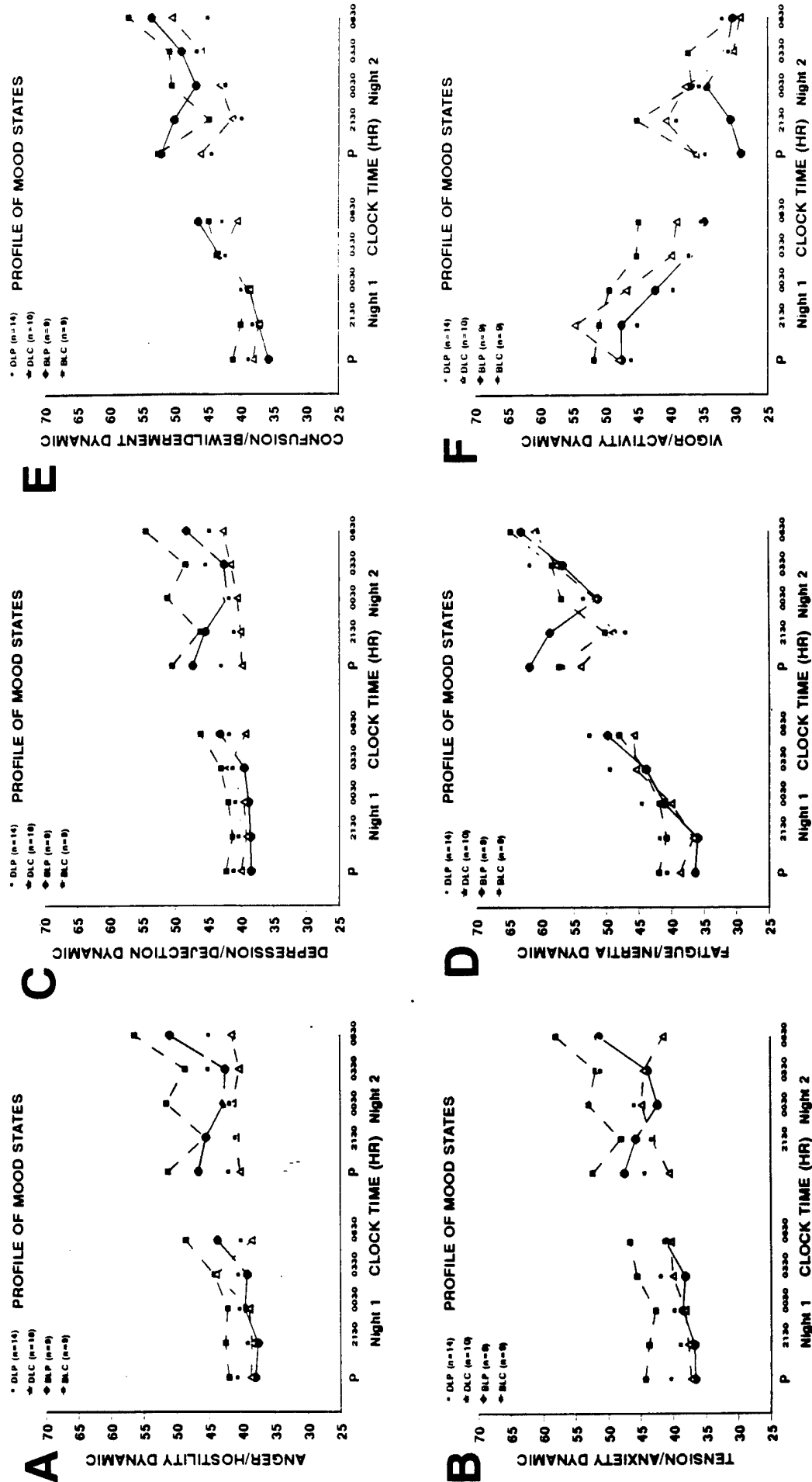


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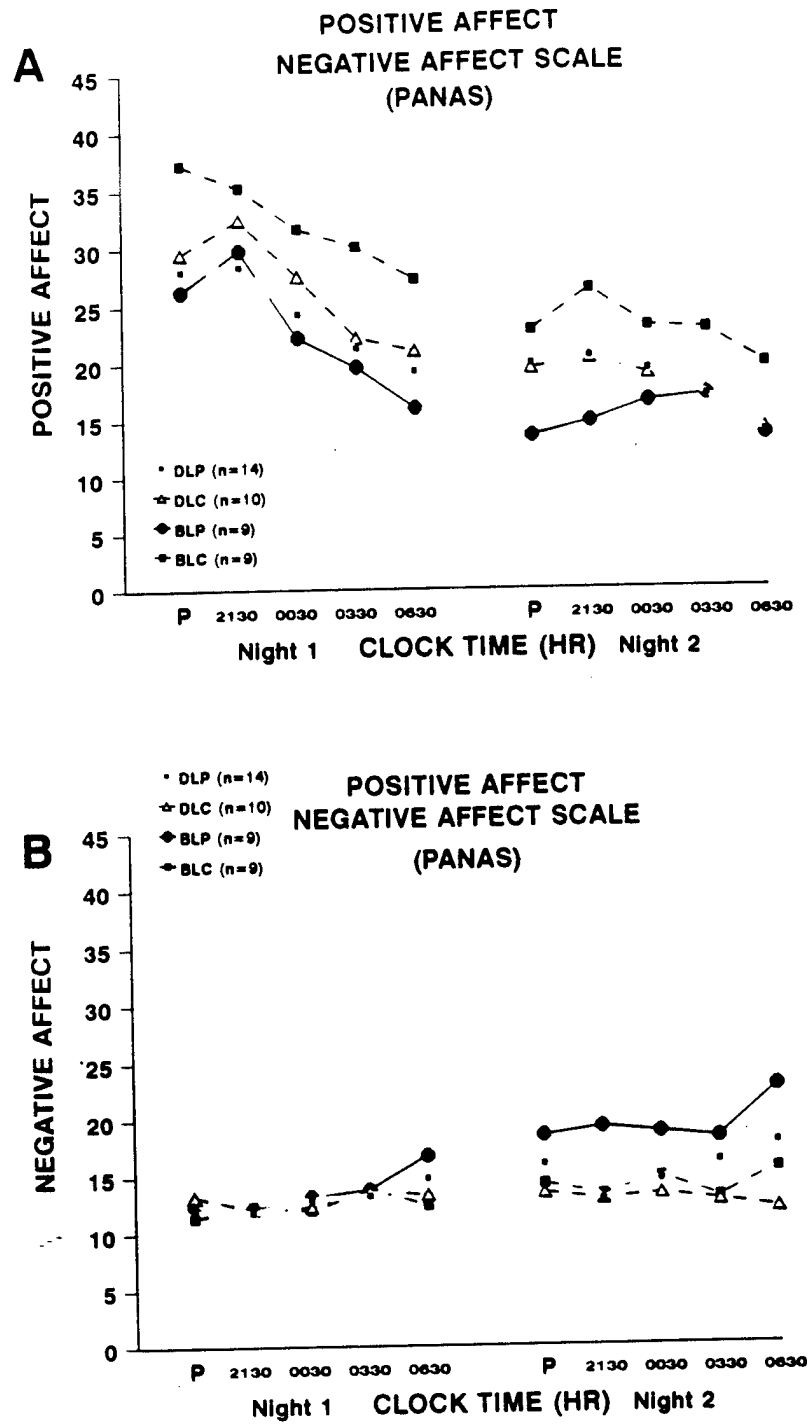


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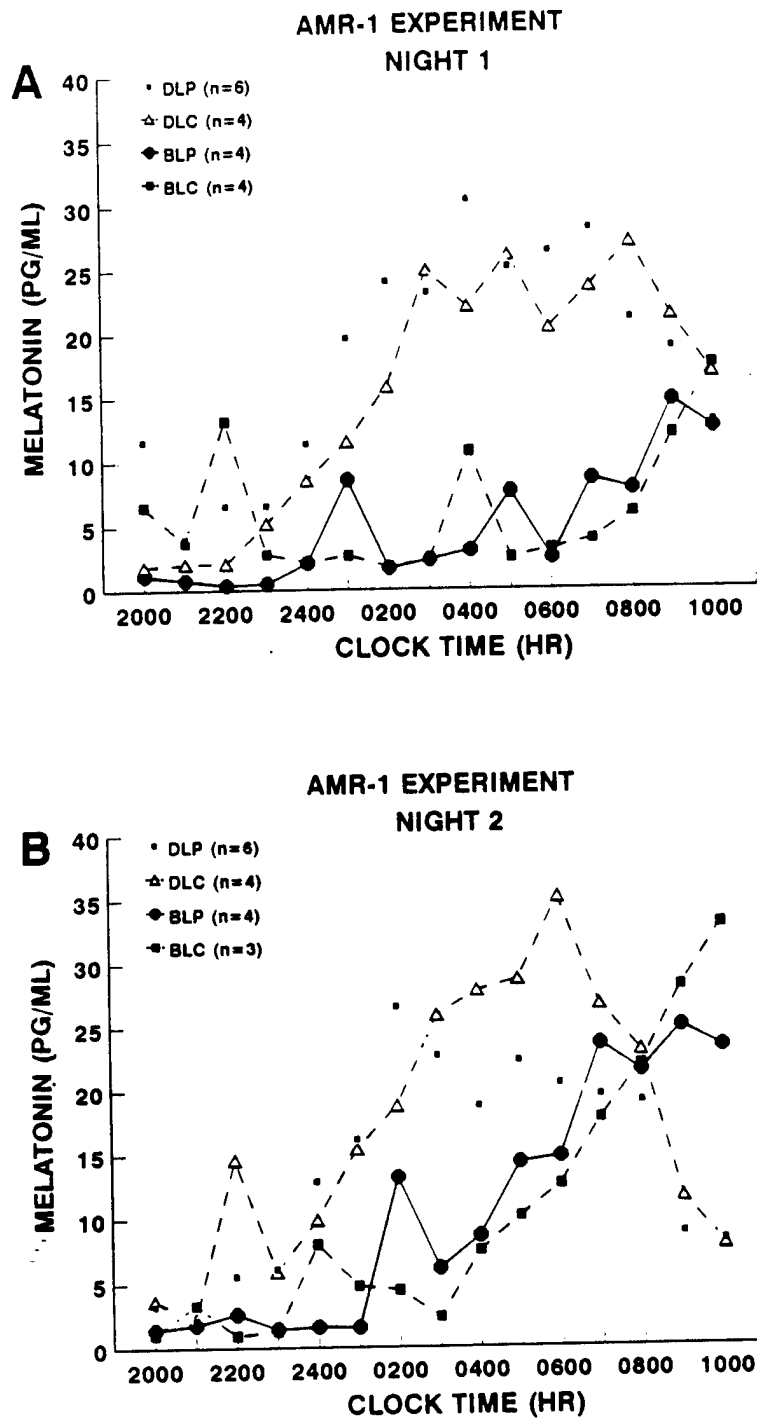


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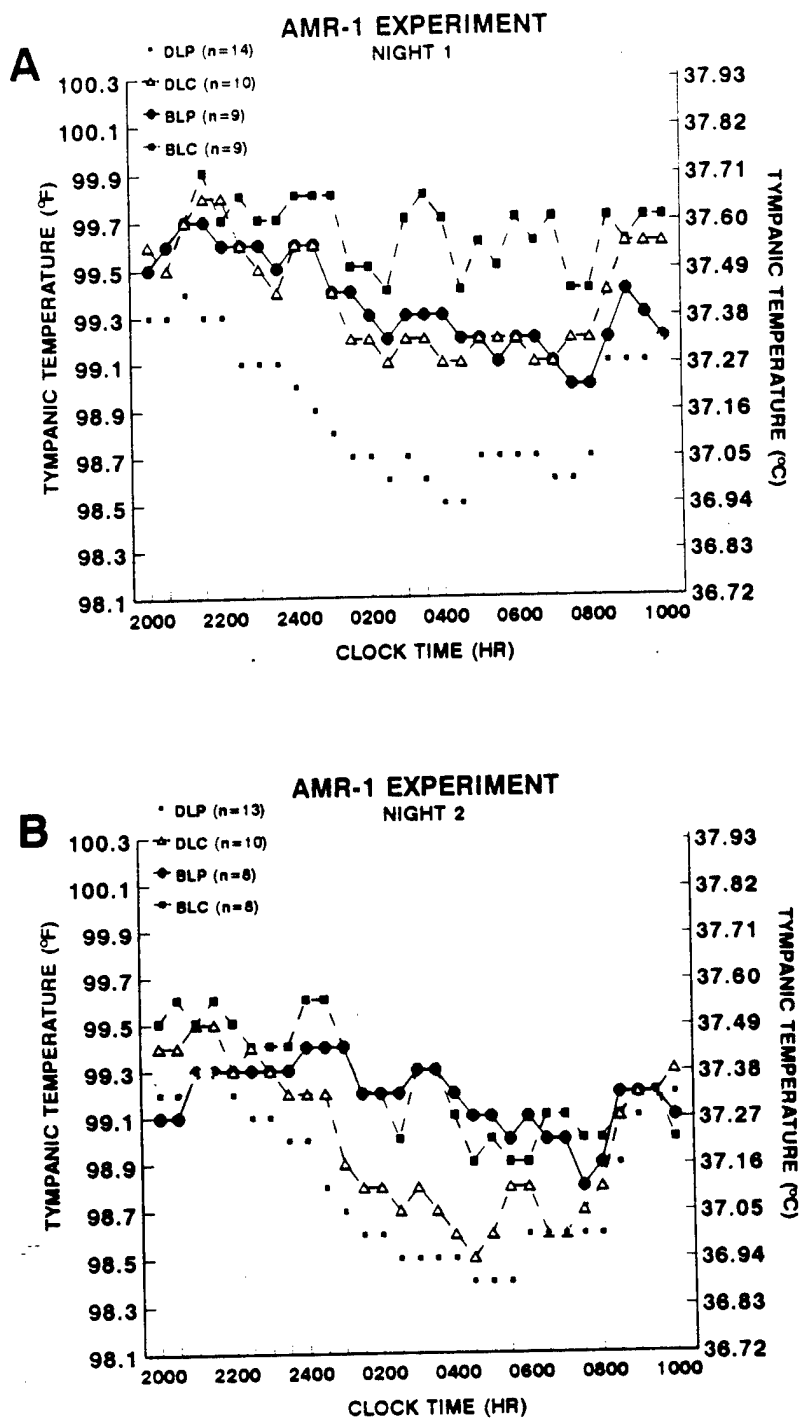


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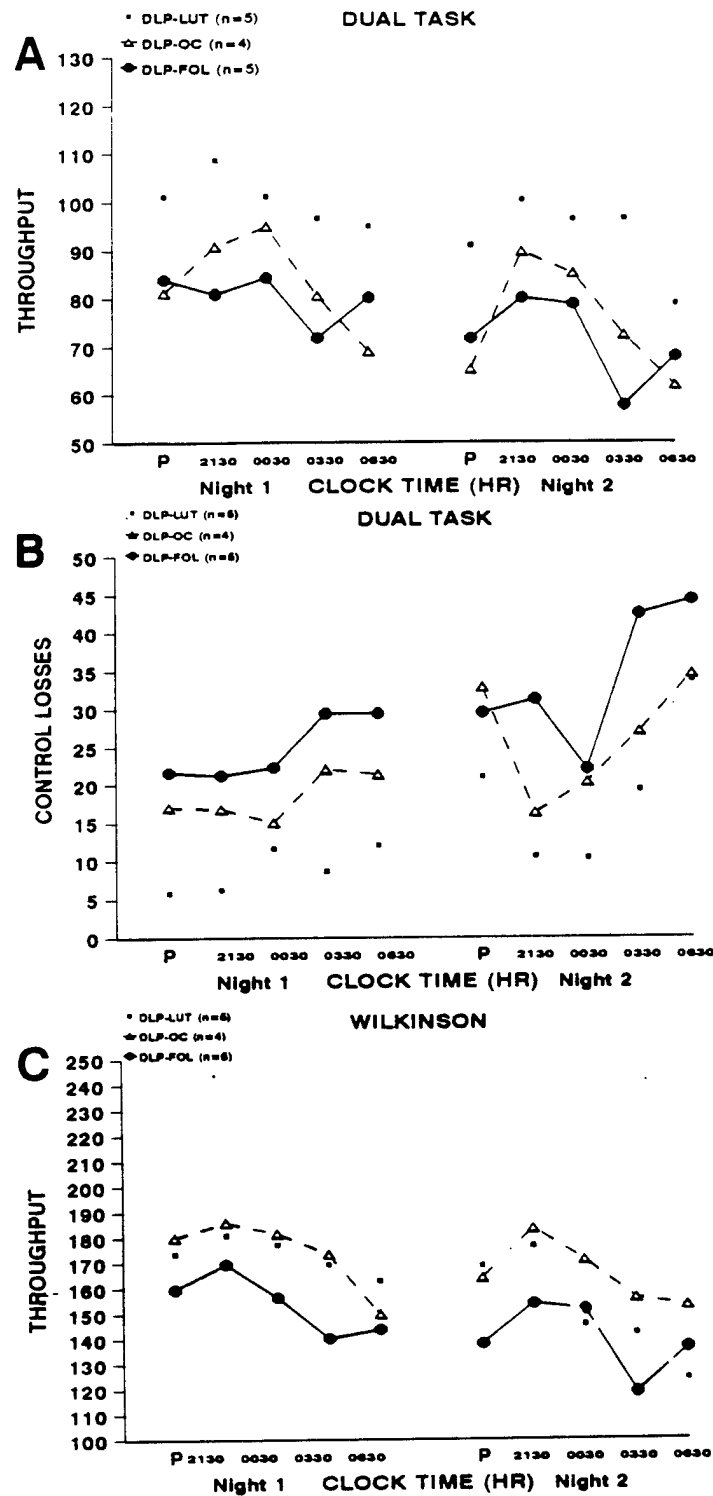


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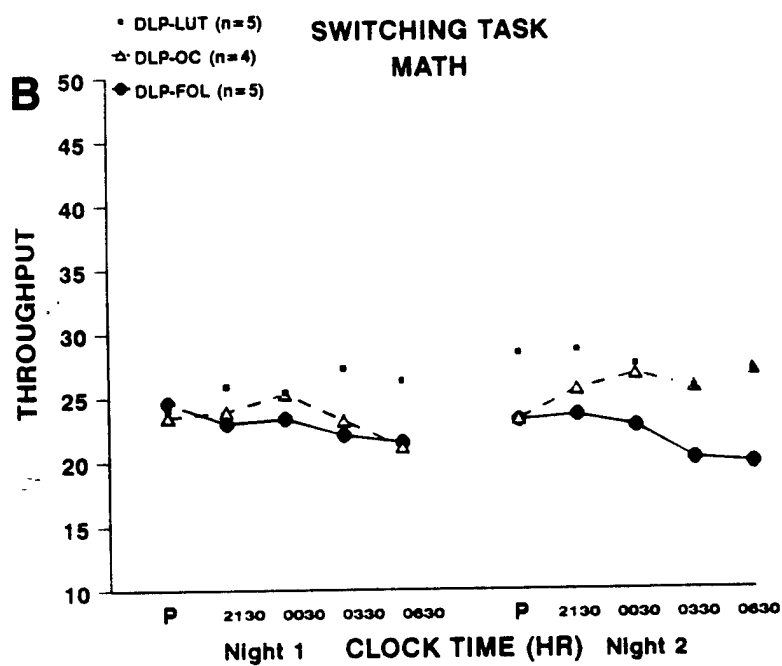
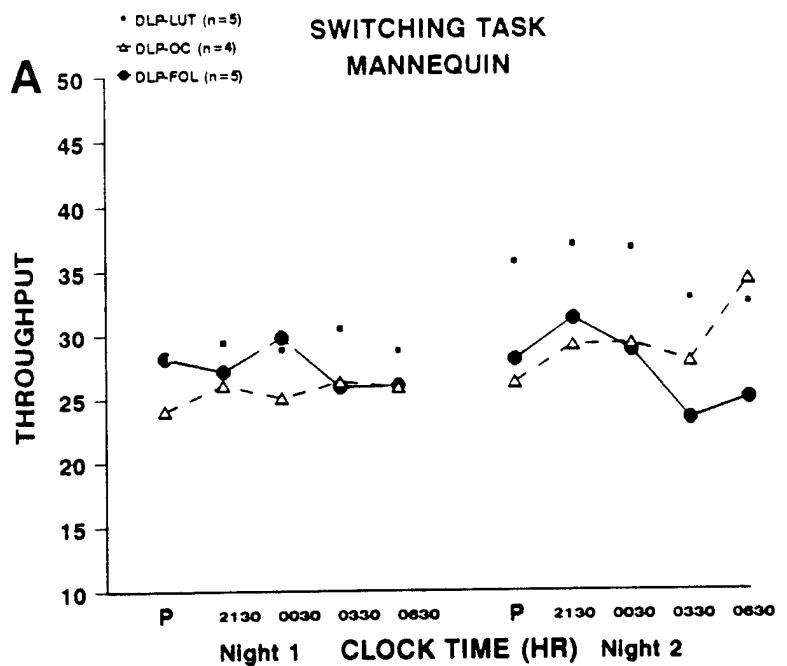


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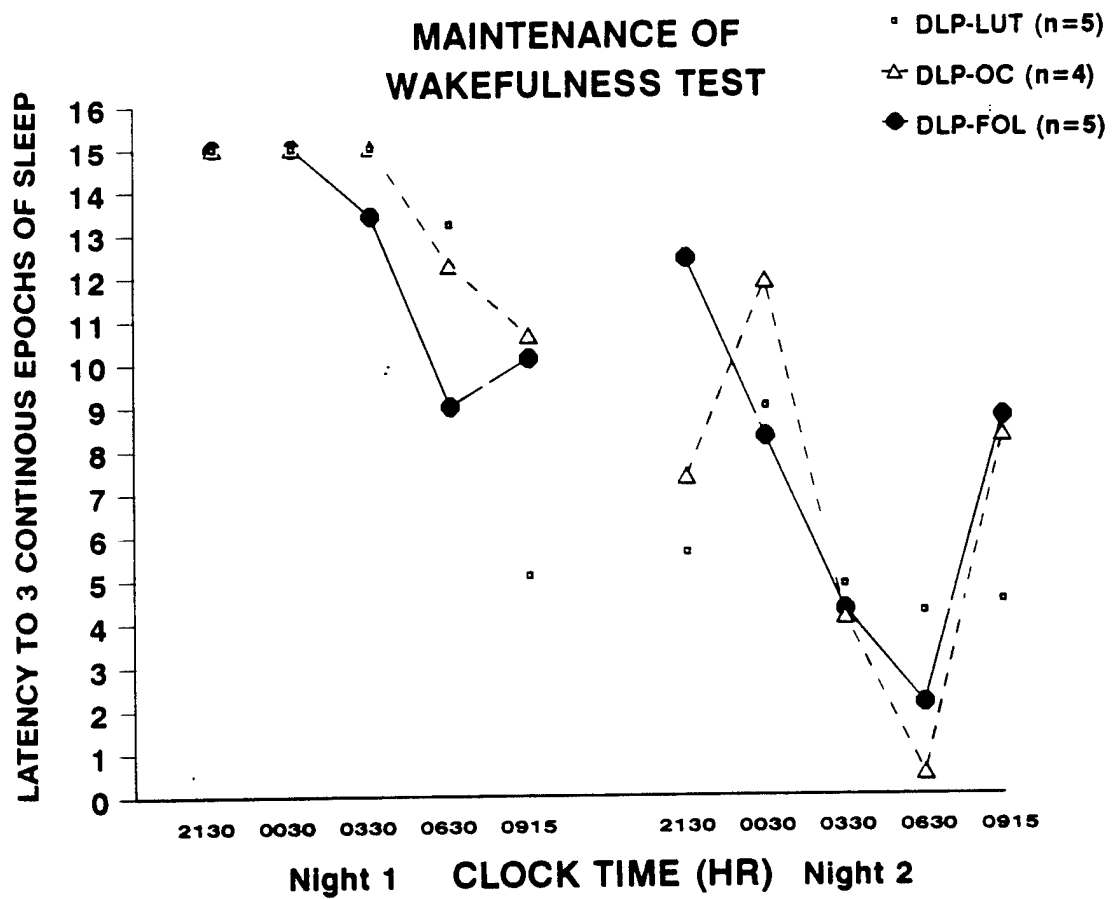
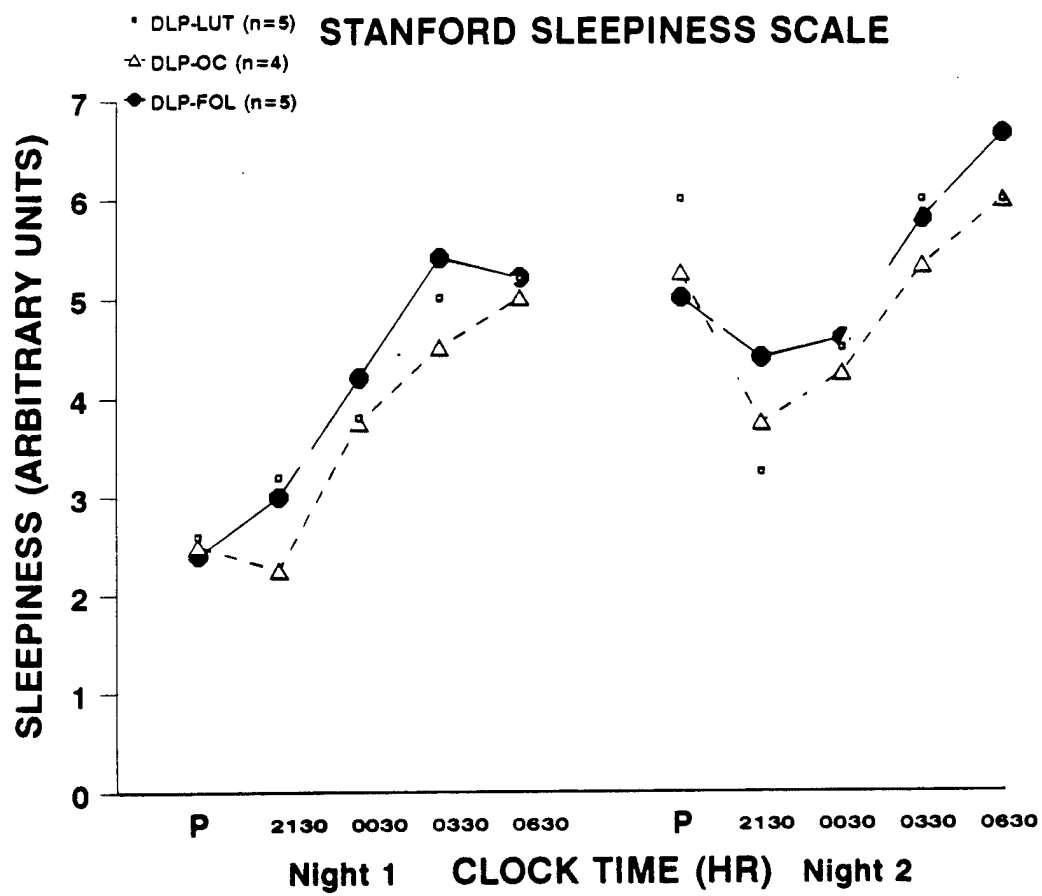


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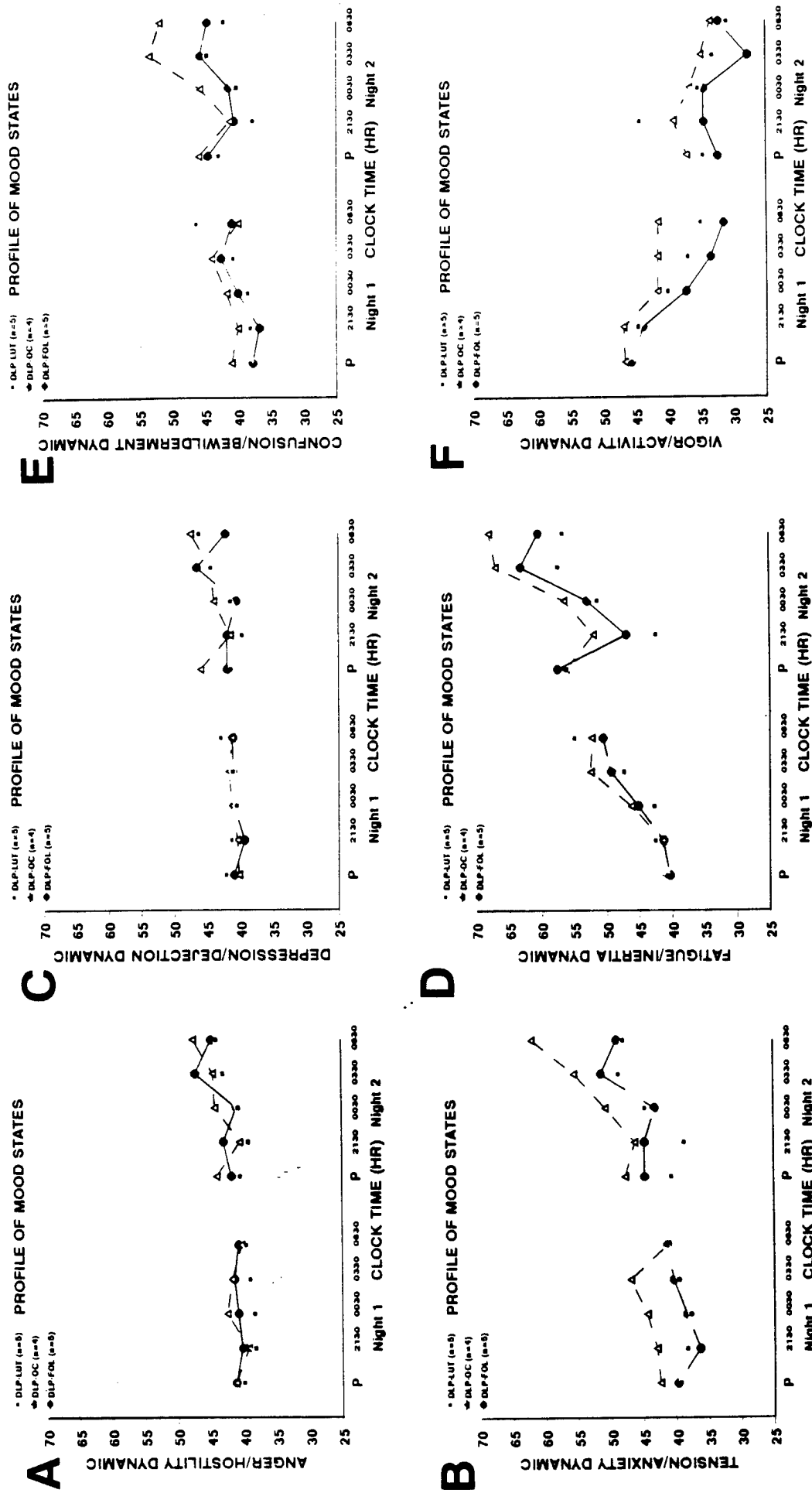


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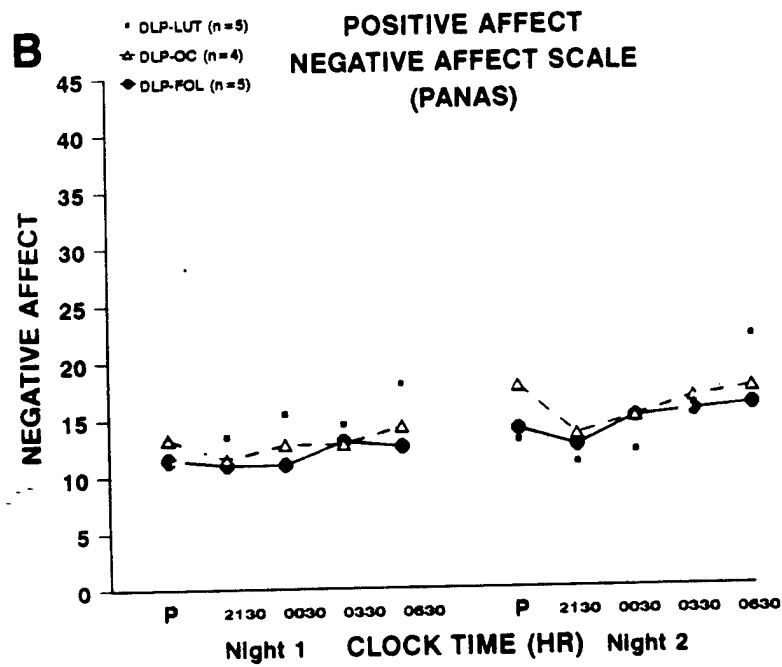
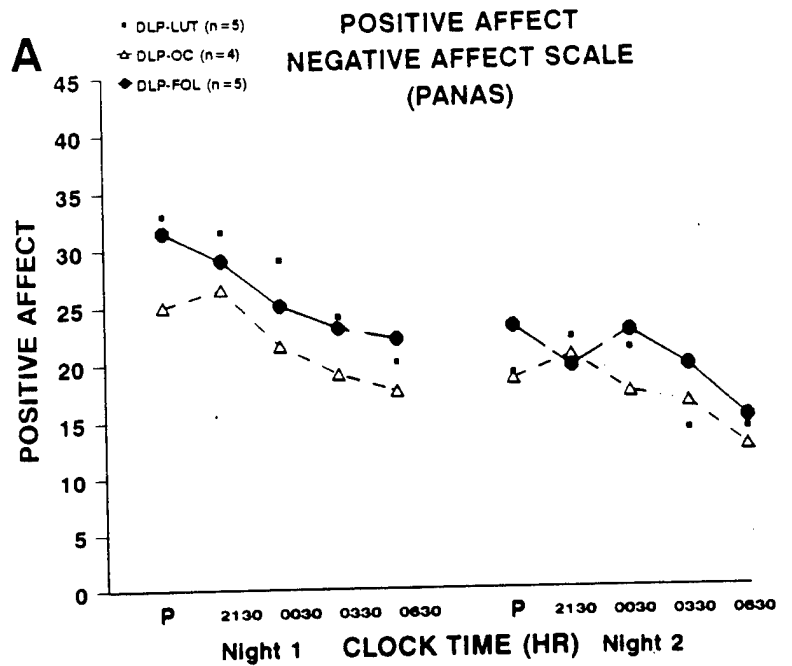


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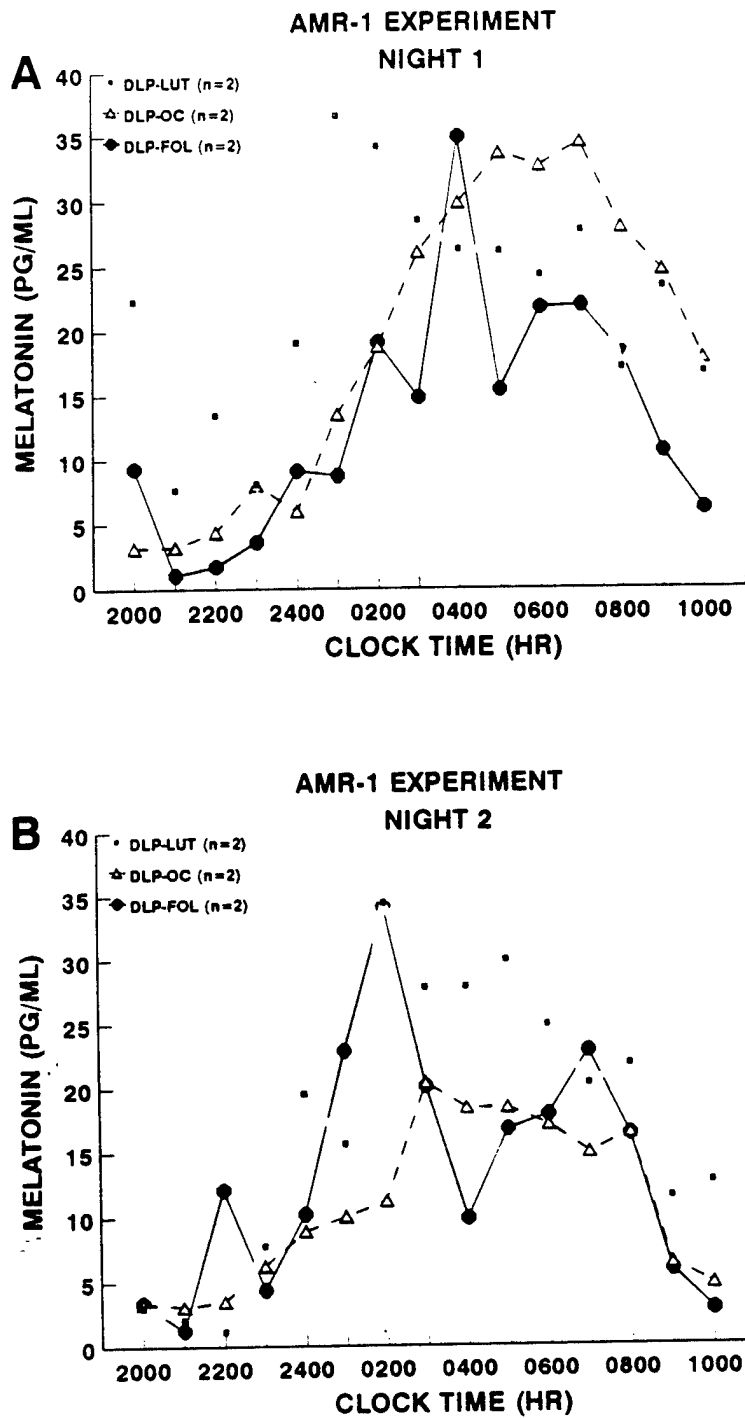


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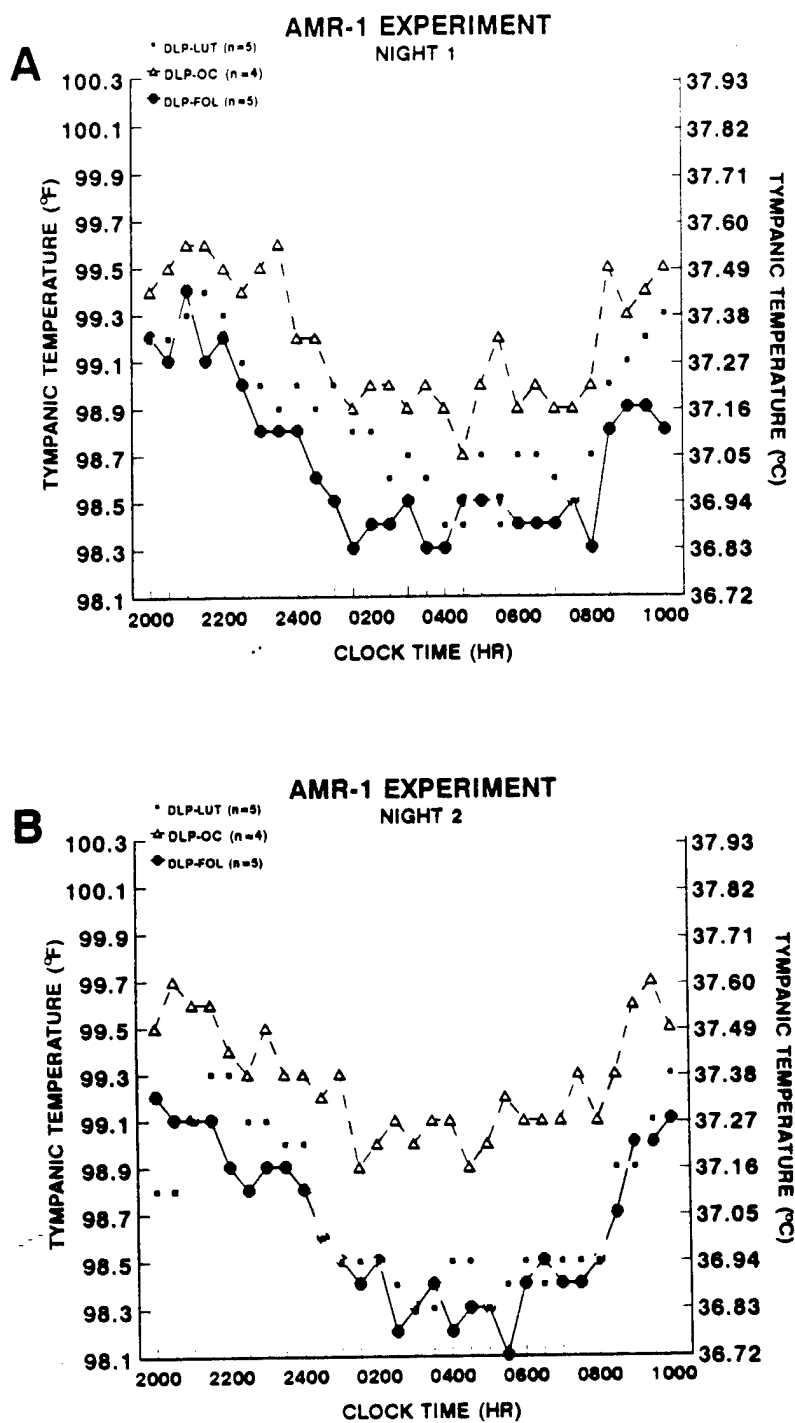


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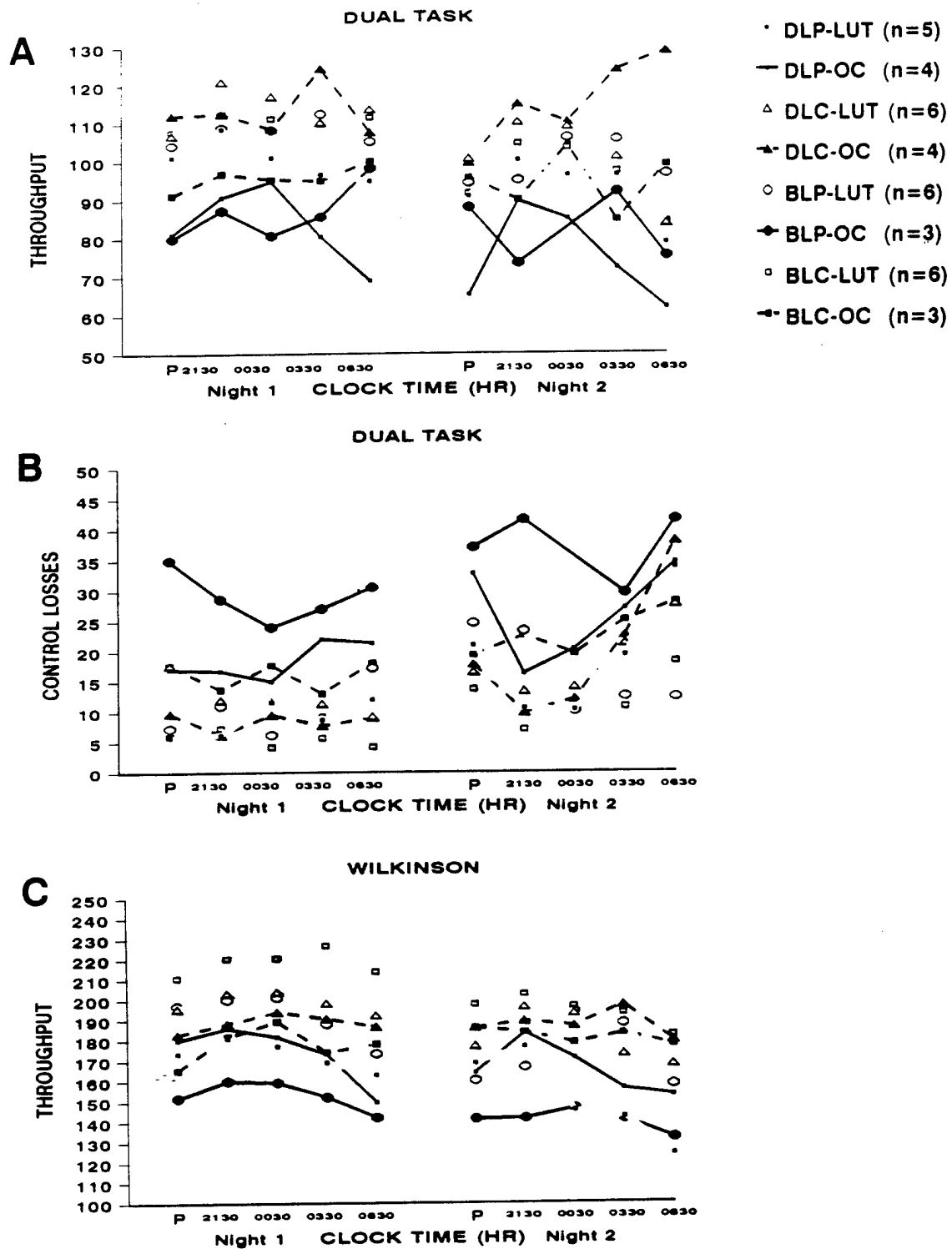


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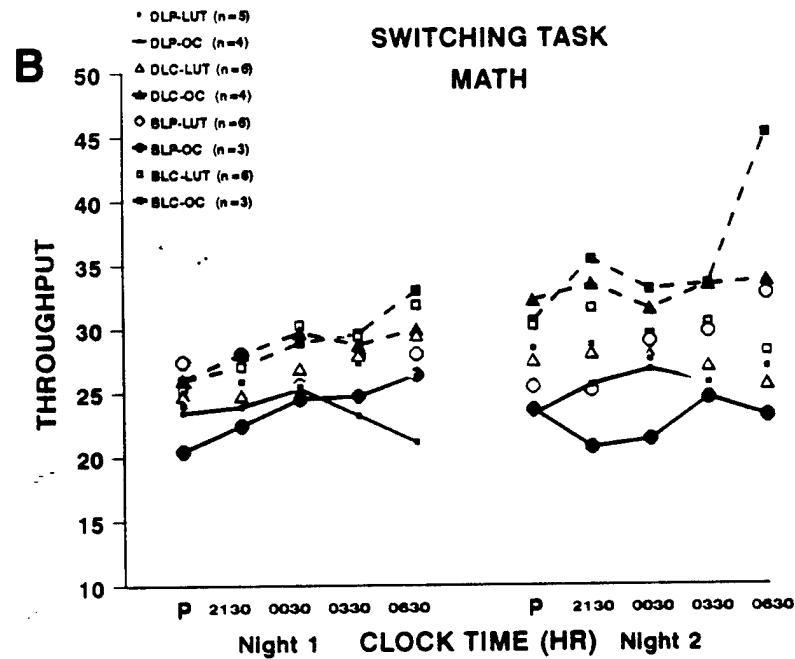
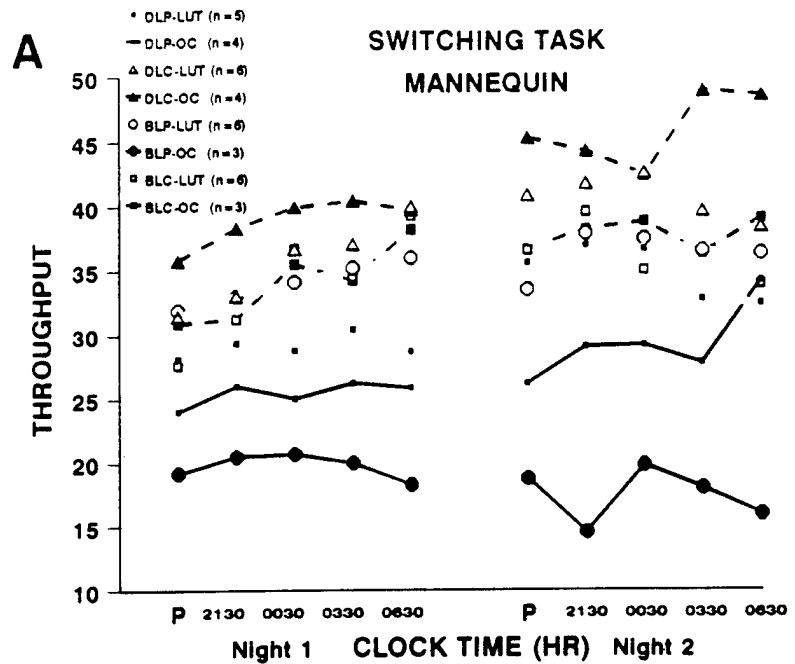


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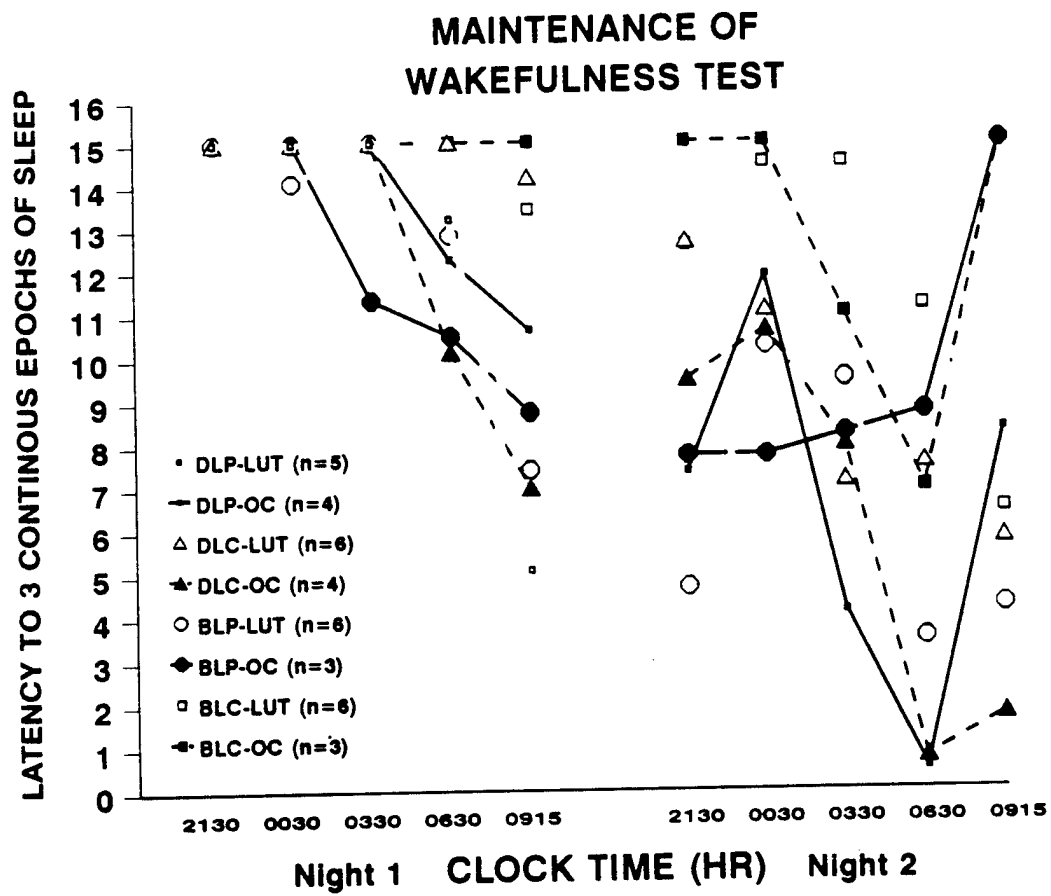
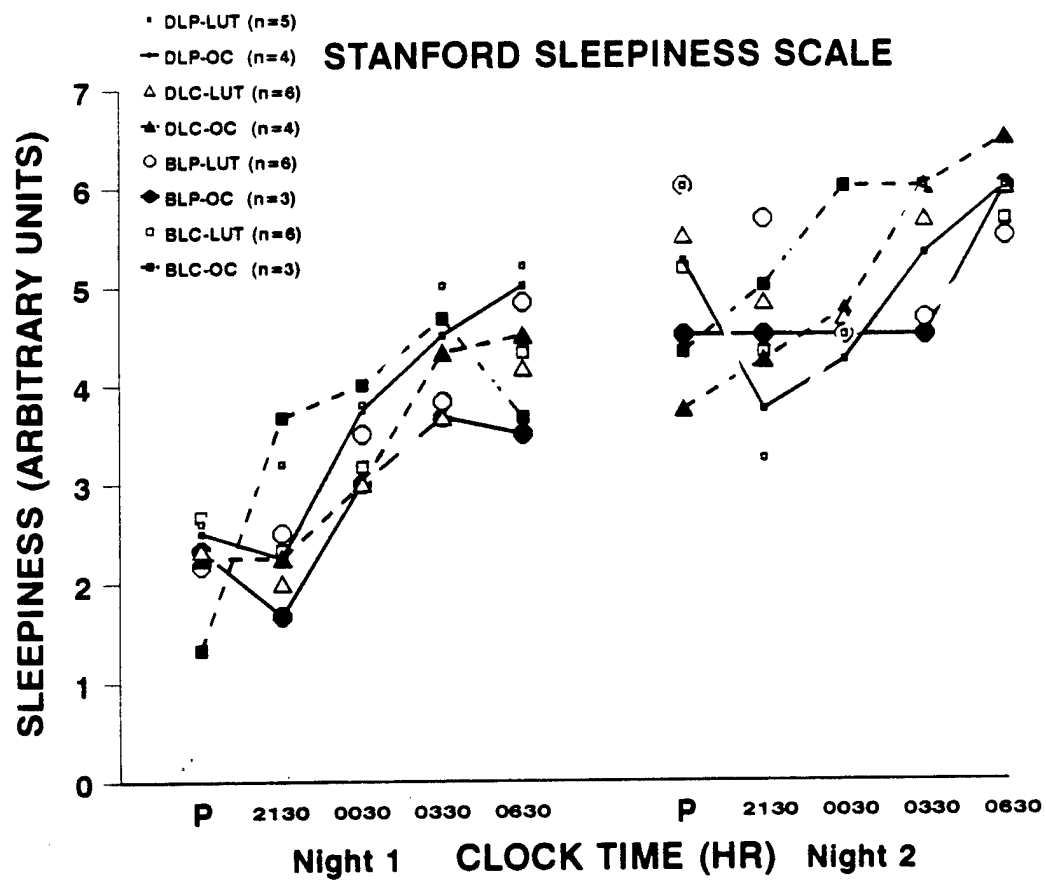


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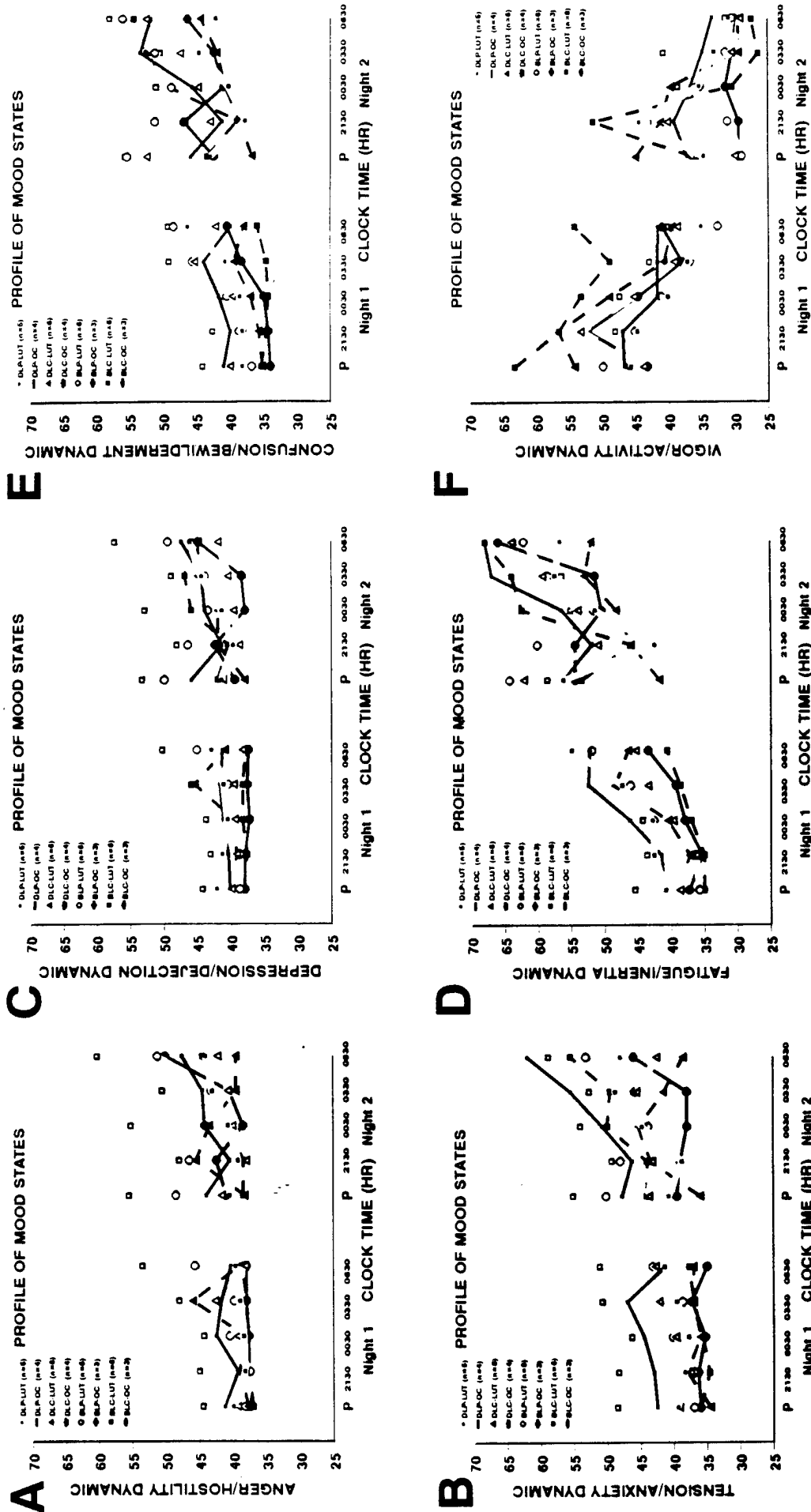
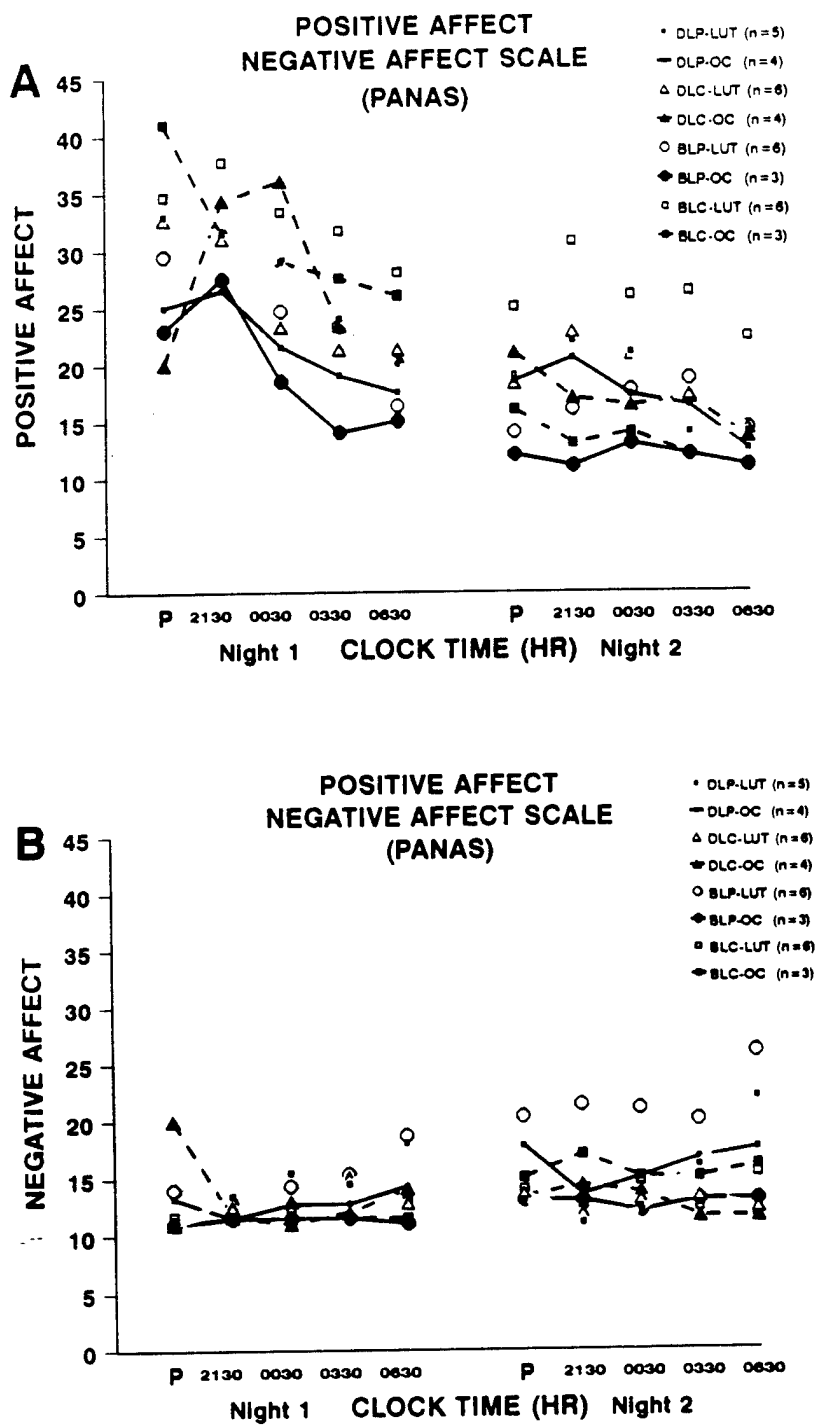


Figure 21

Figure 22



AMR-1 EXPERIMENT
NIGHT 1

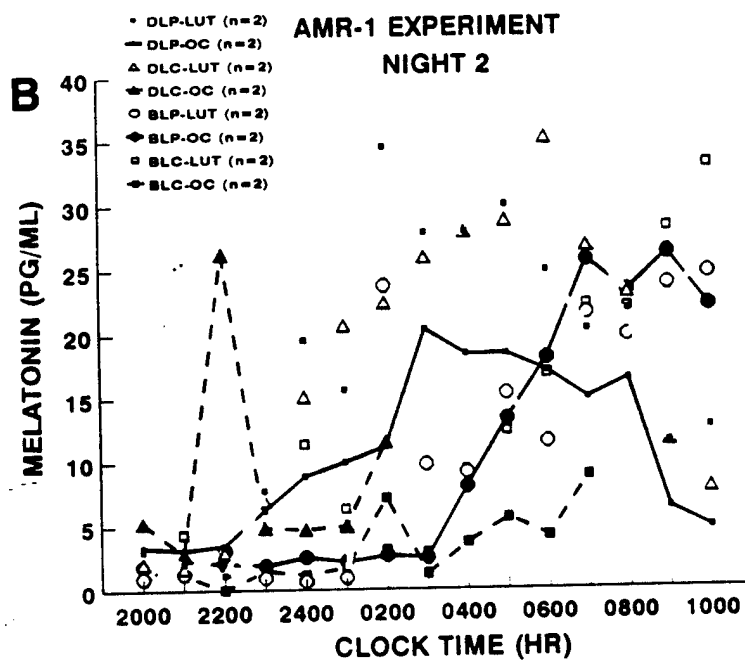


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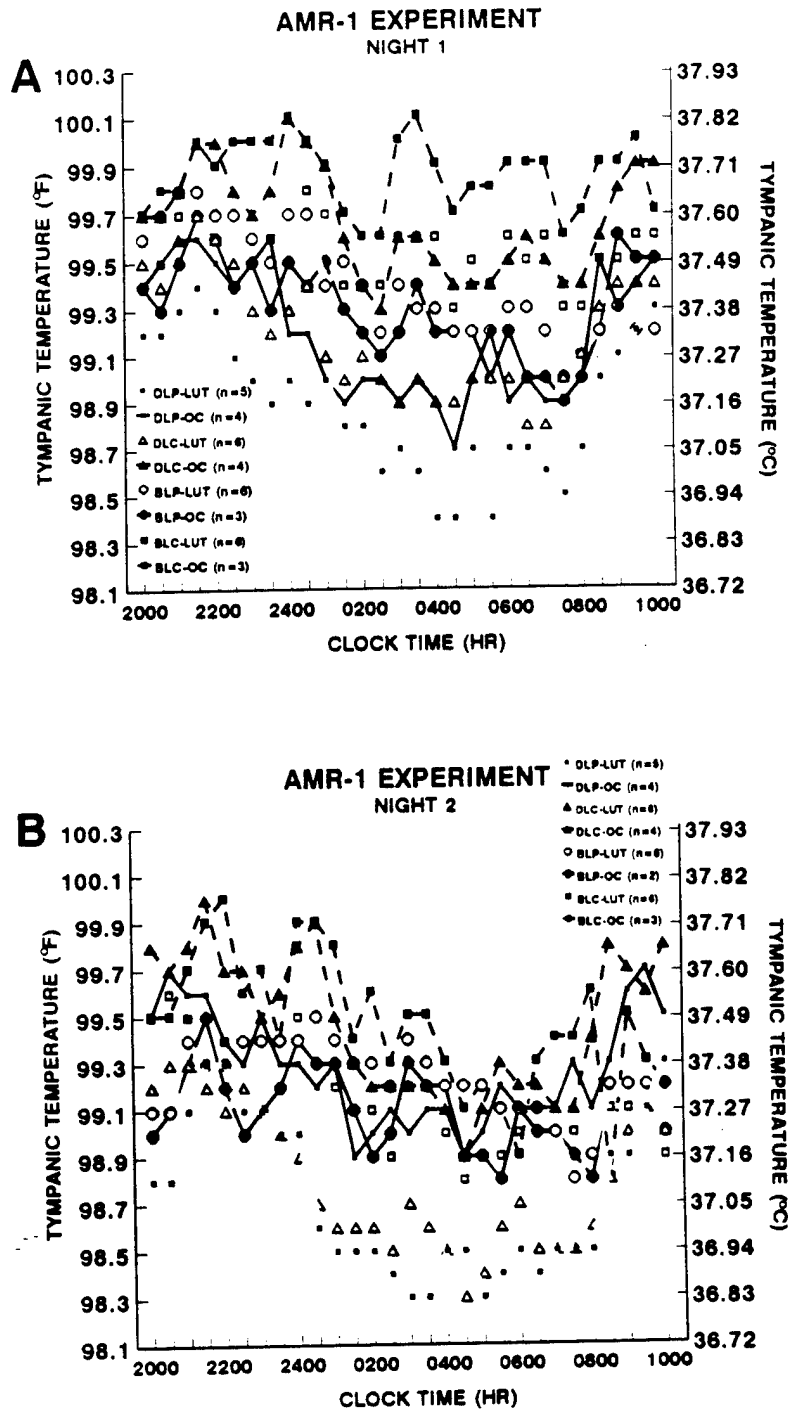
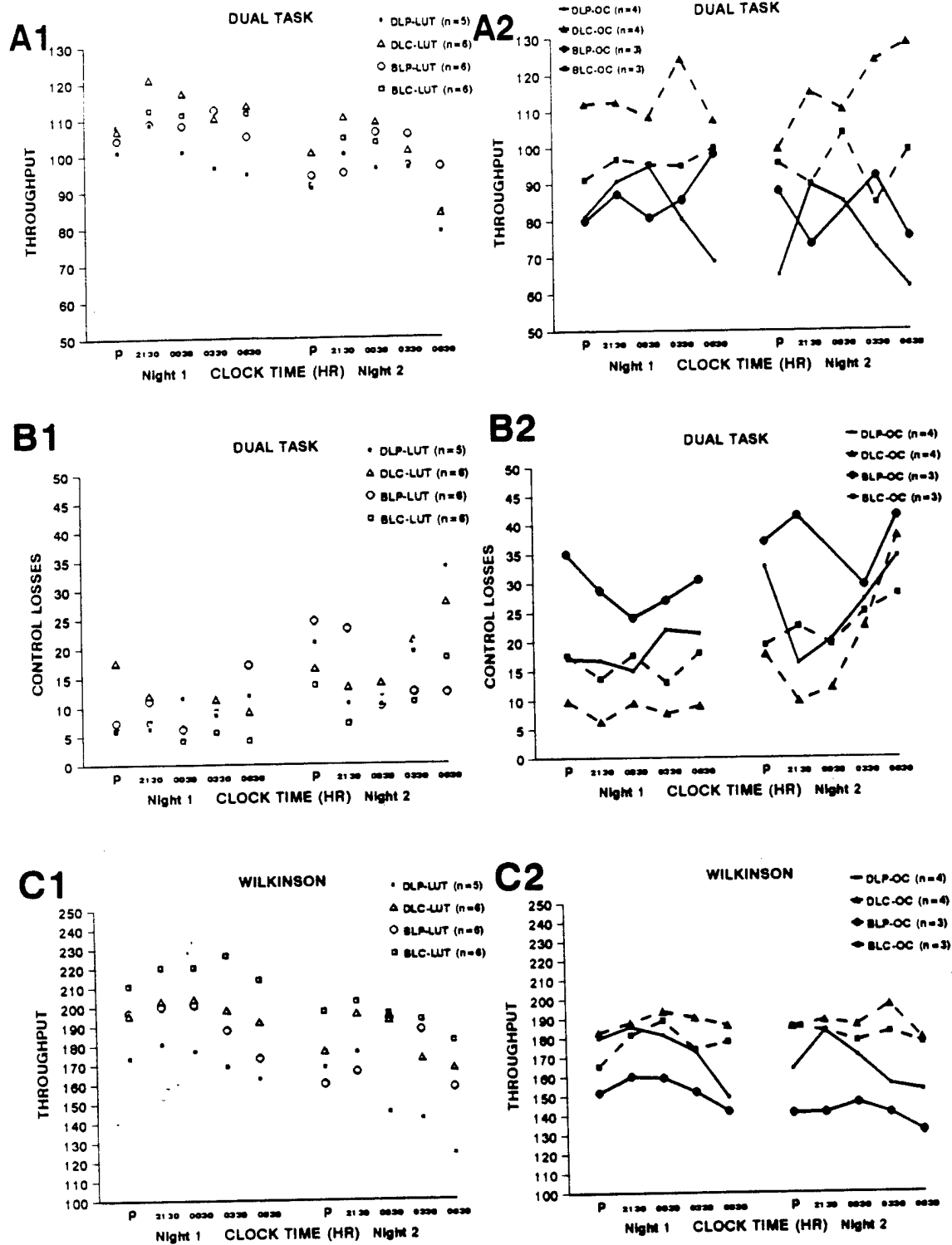


Figure A17



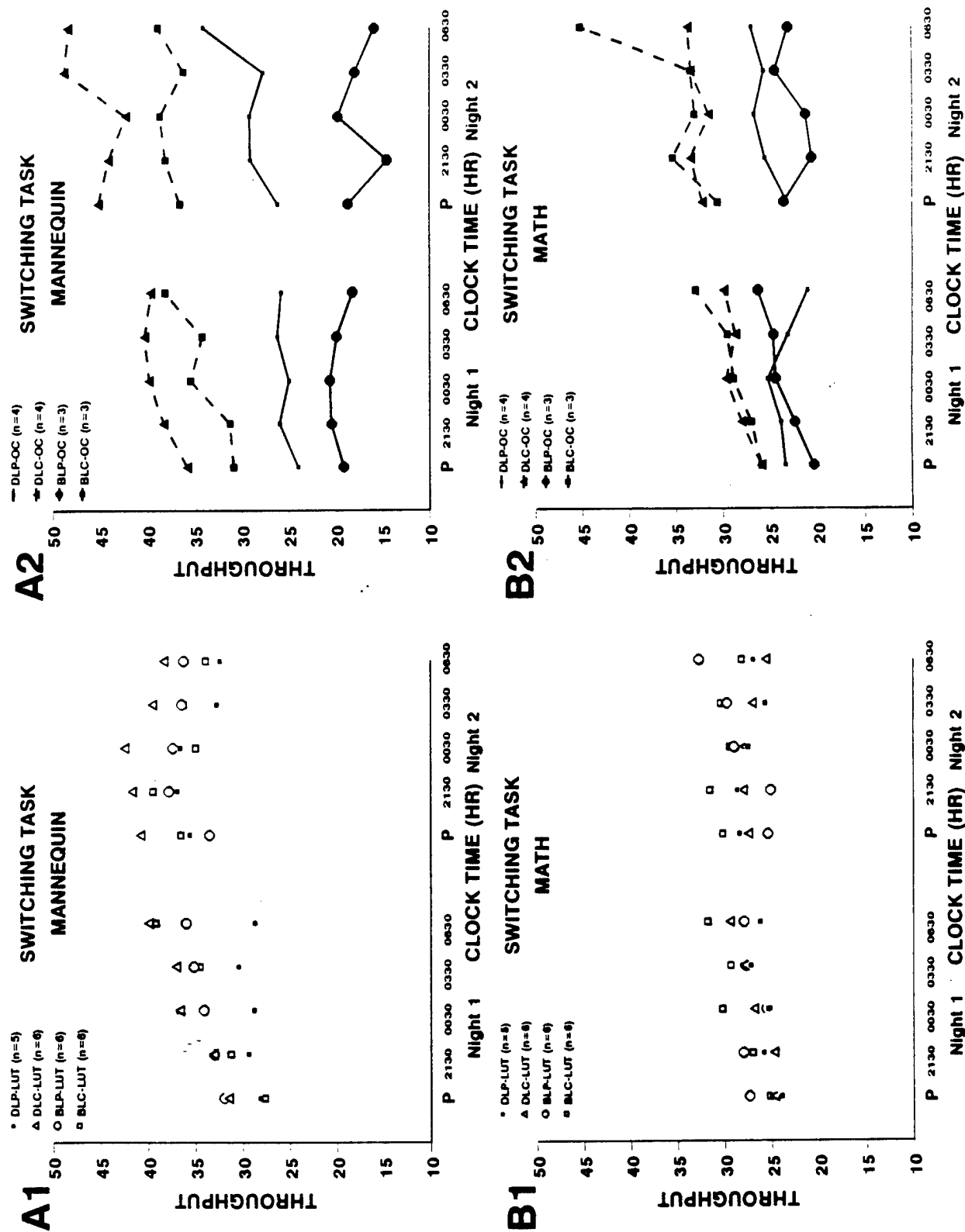


Figure A18

Figure A19

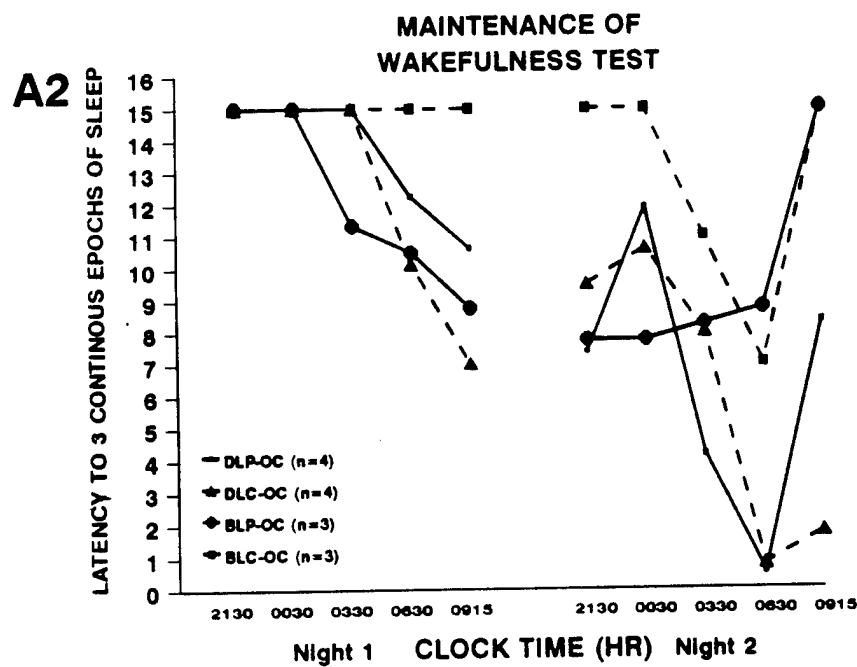
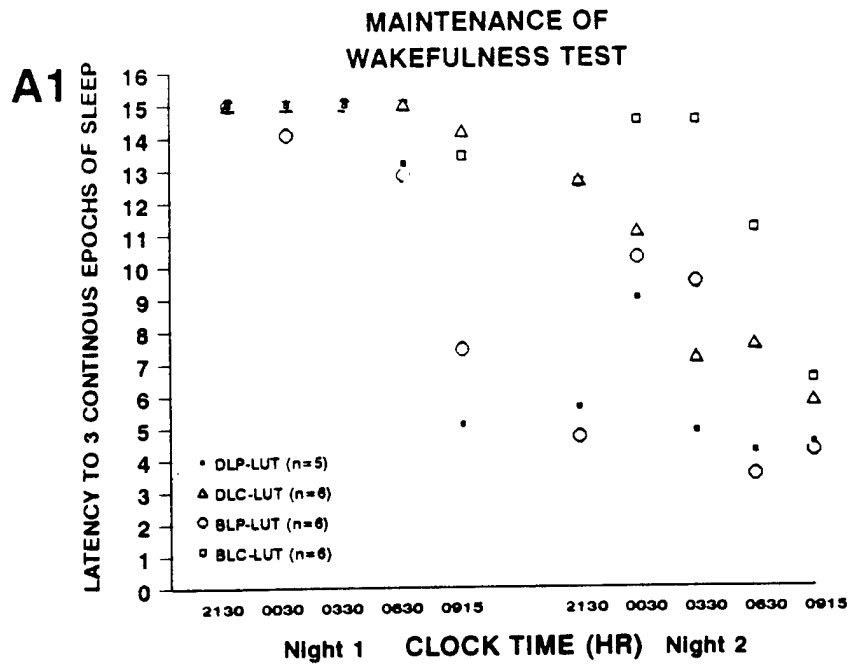


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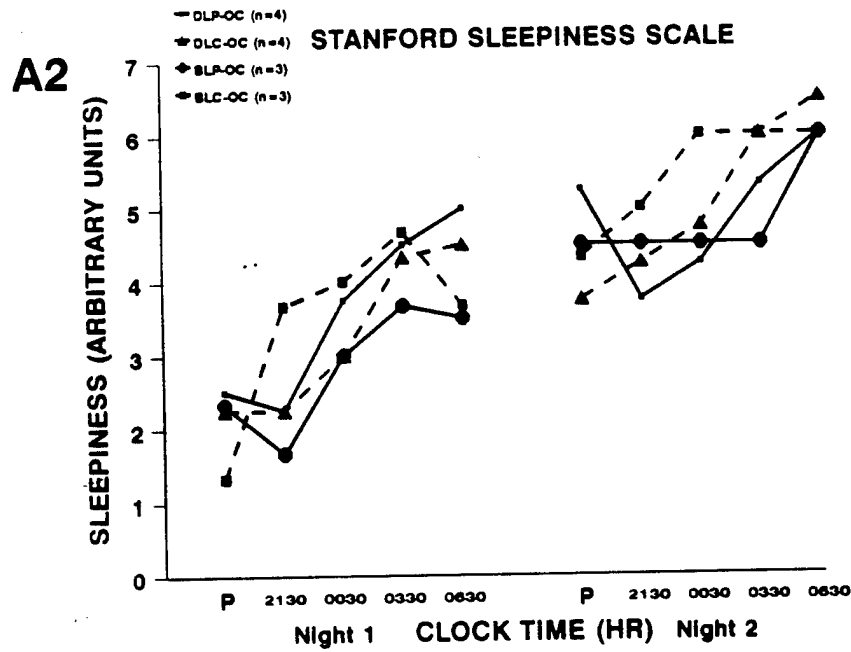
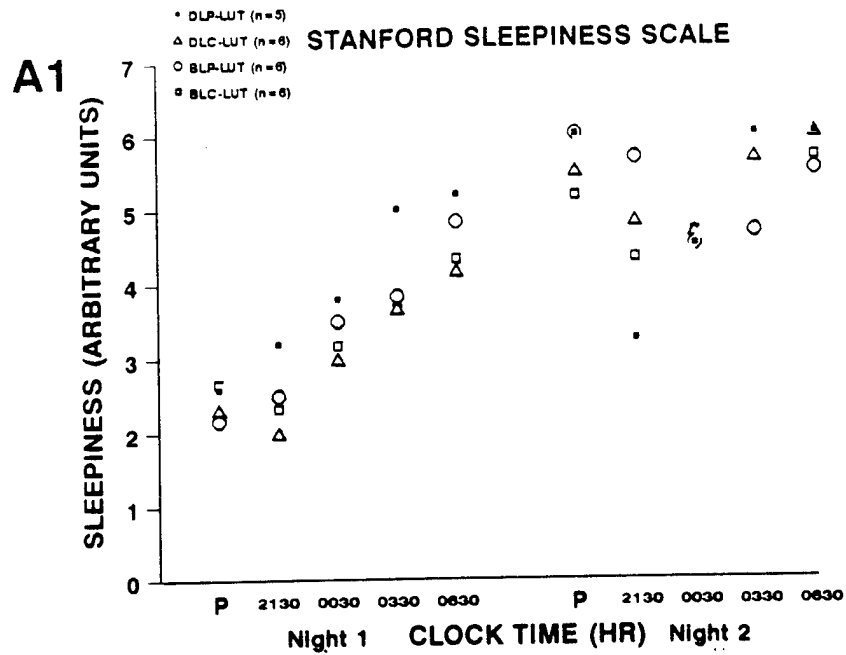


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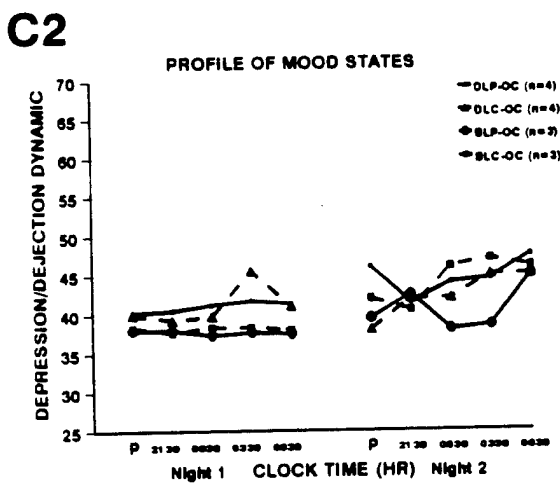
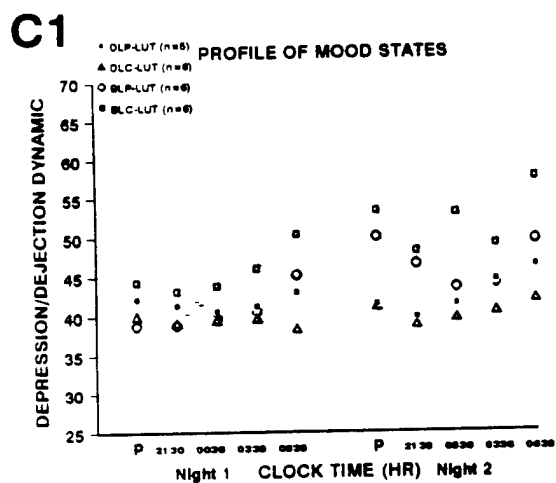
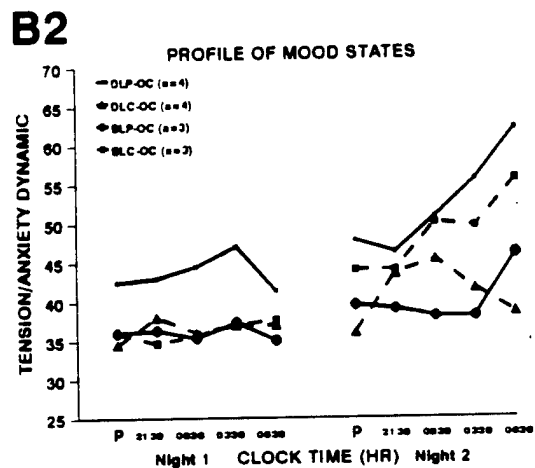
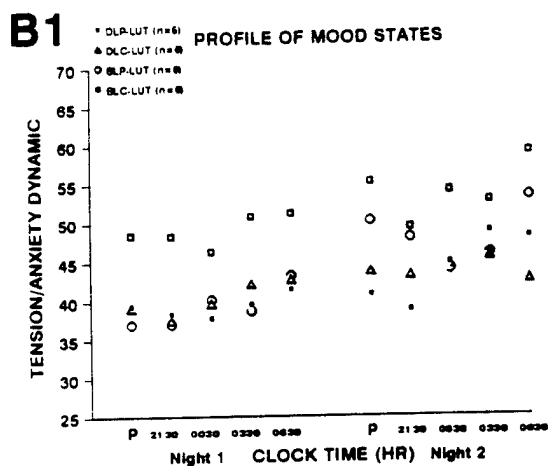
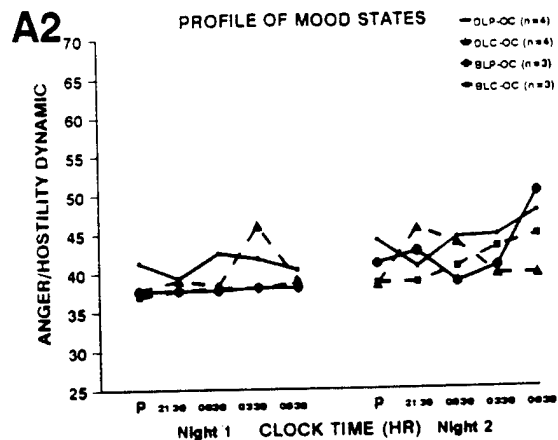
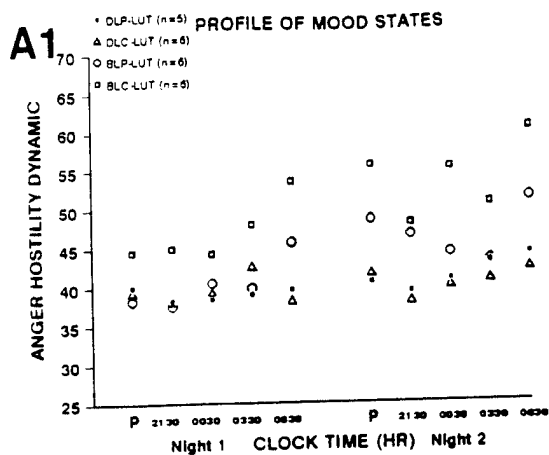
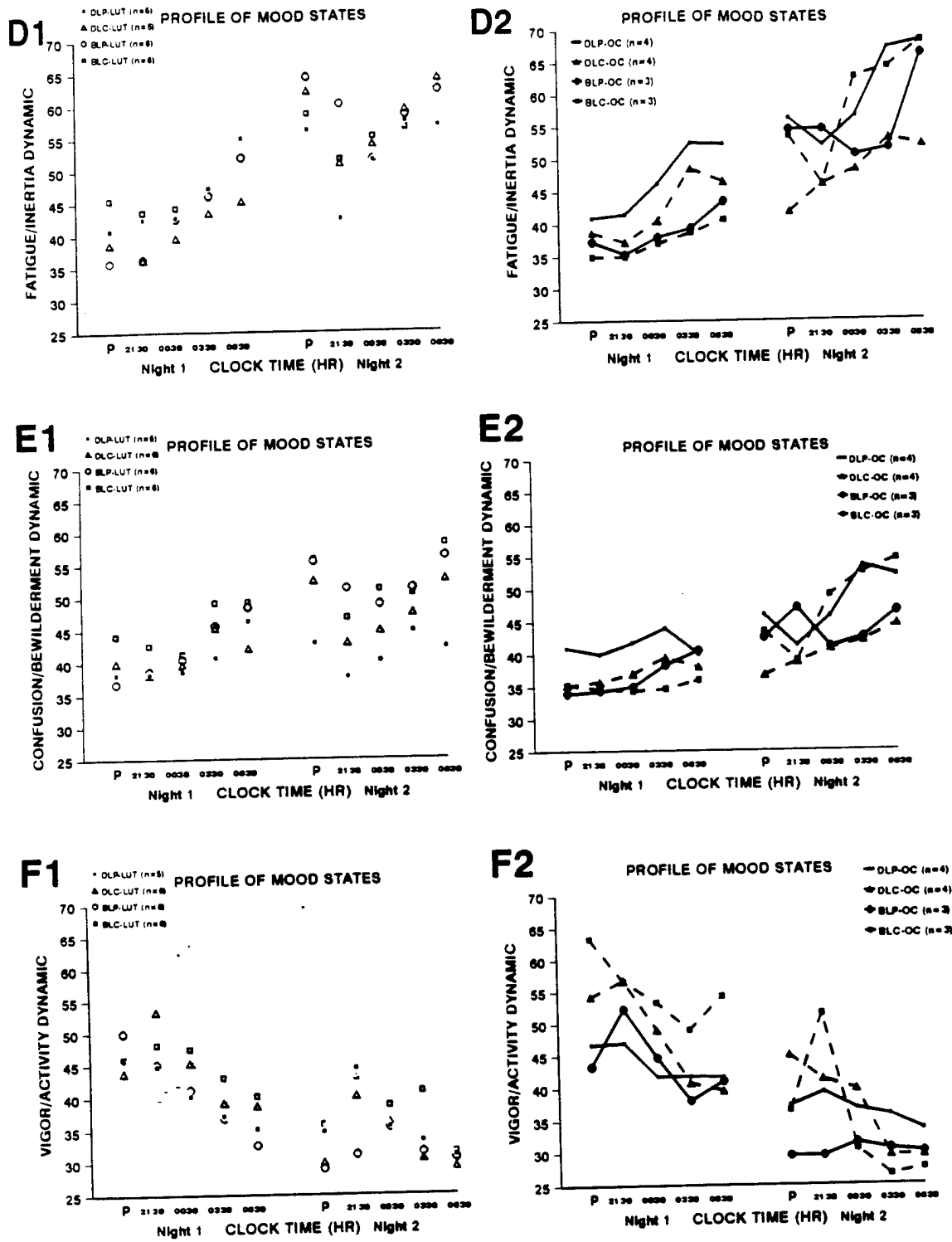


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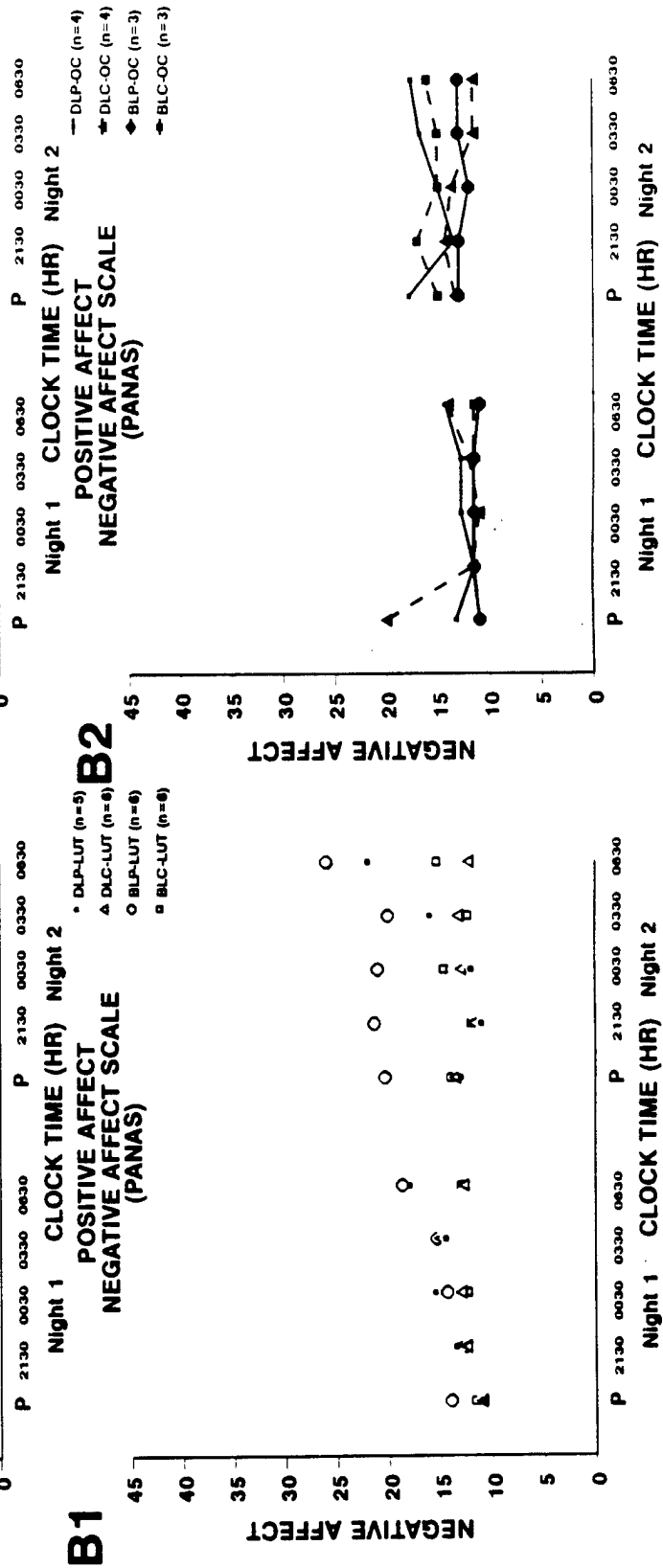
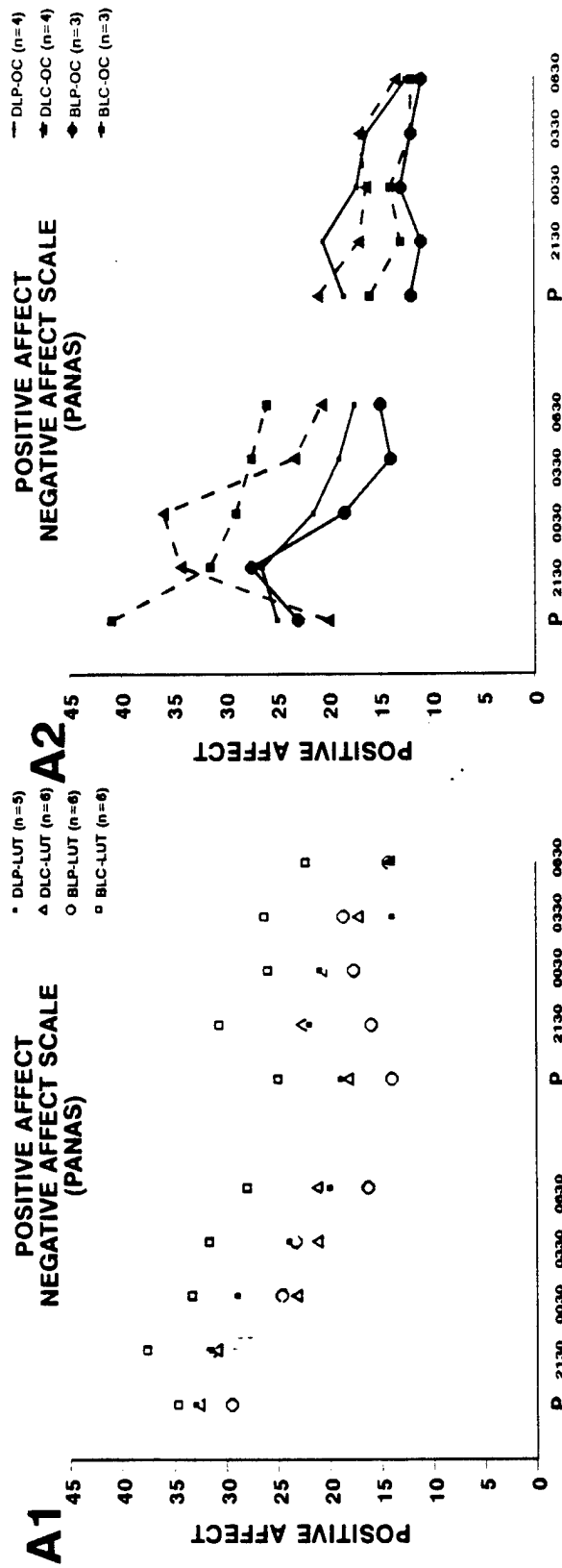


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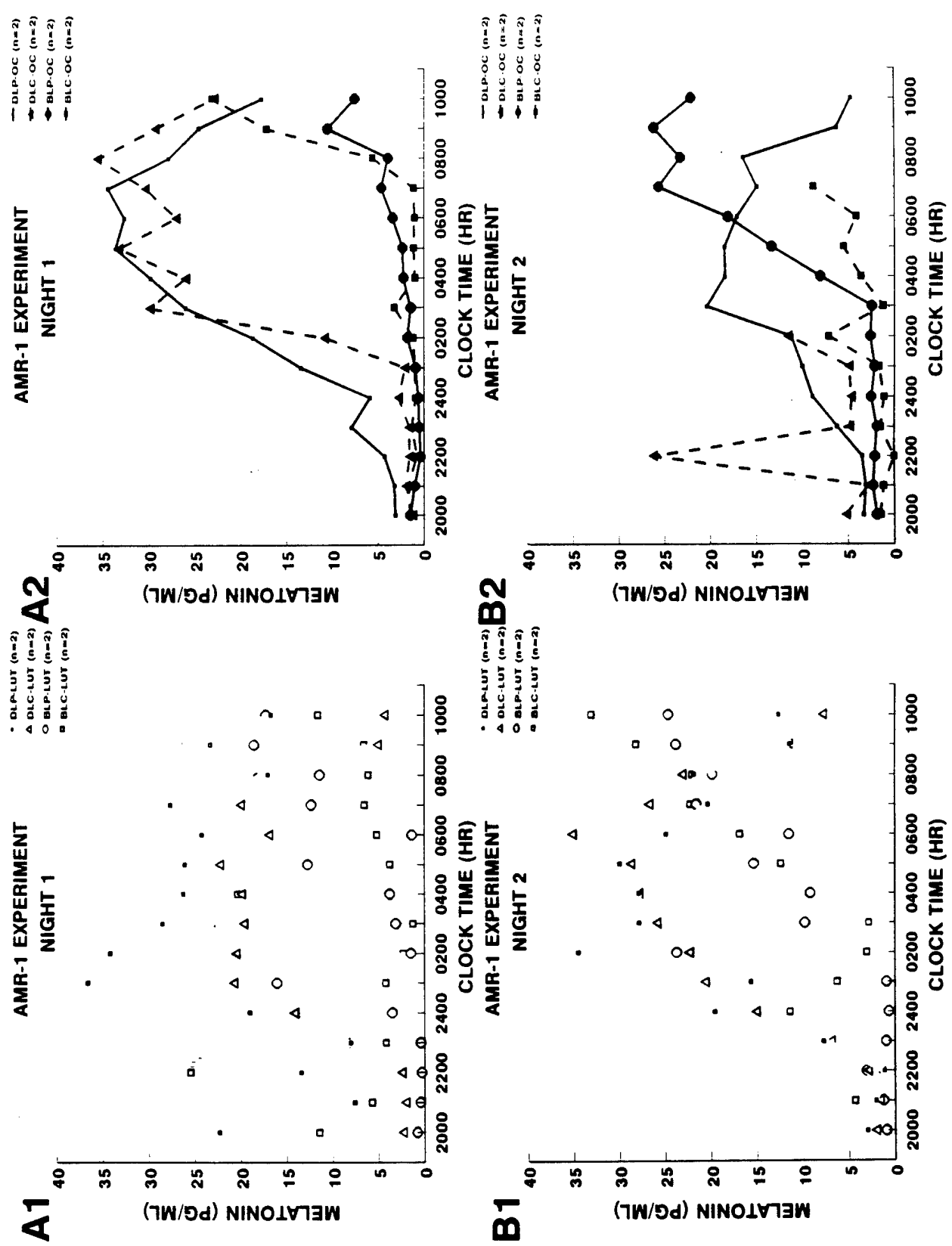


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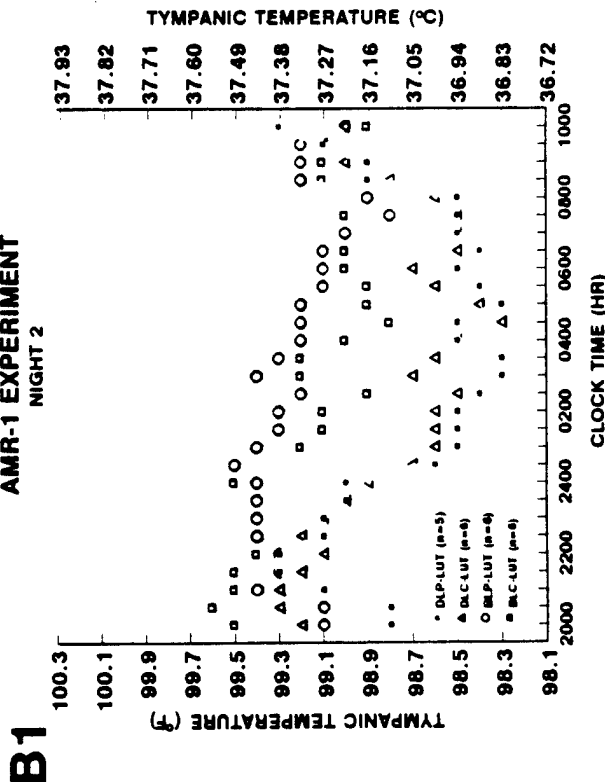
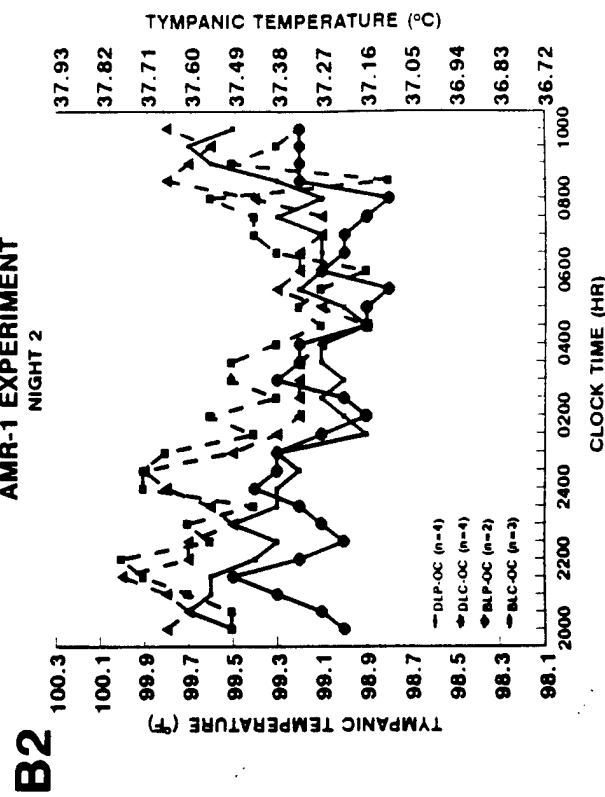
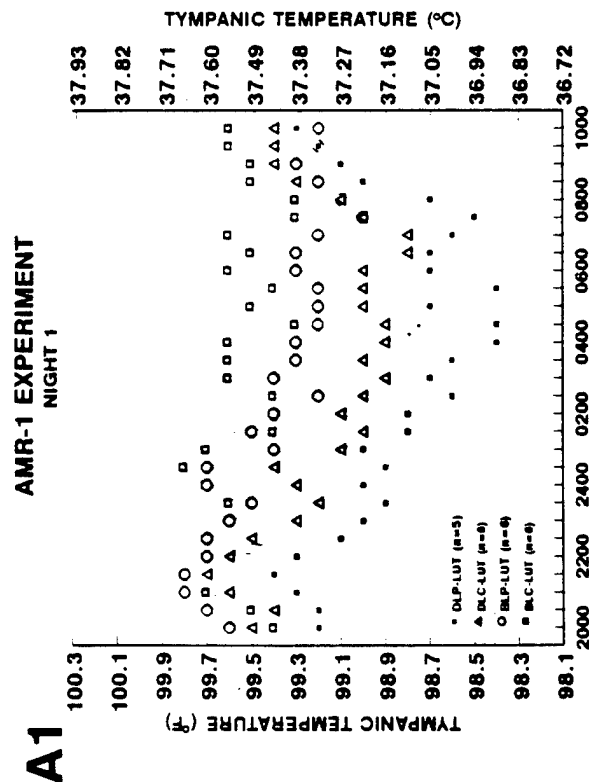
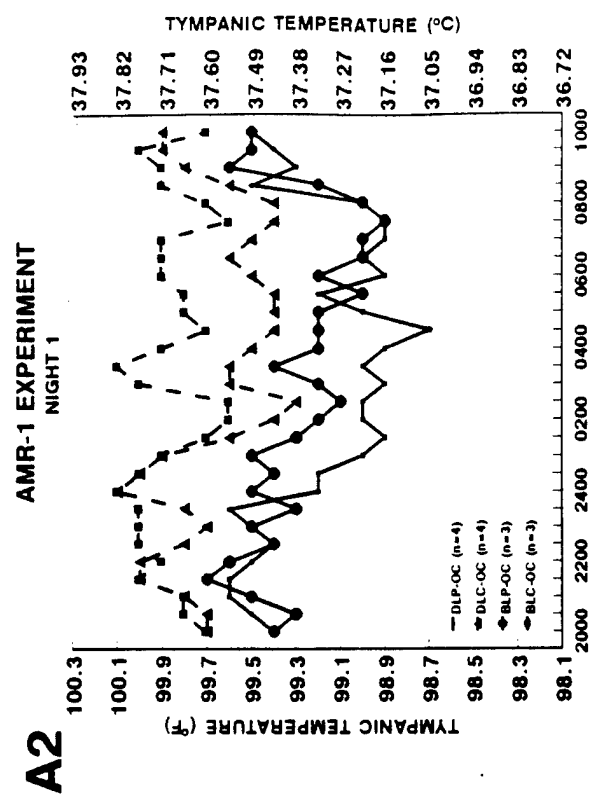


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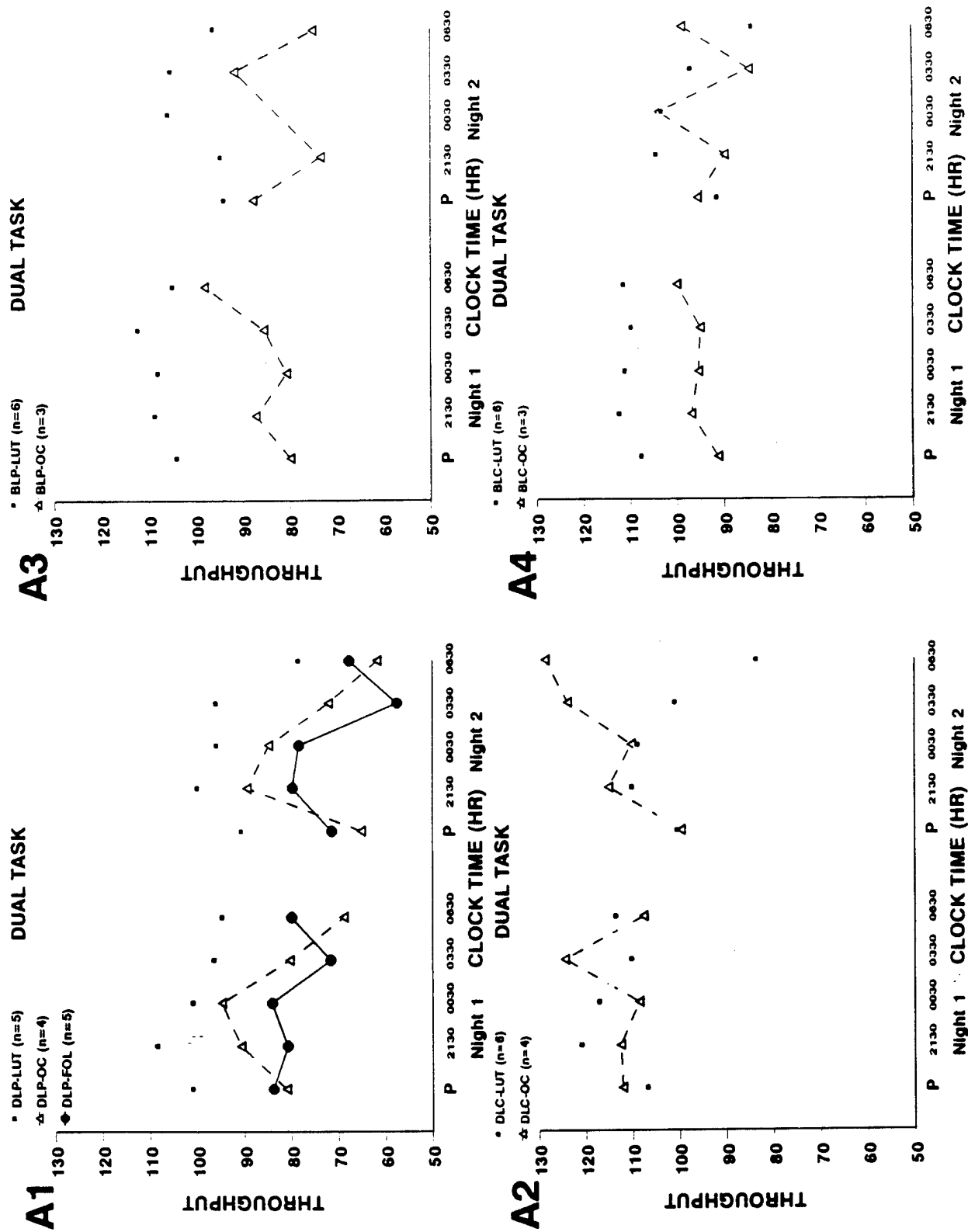


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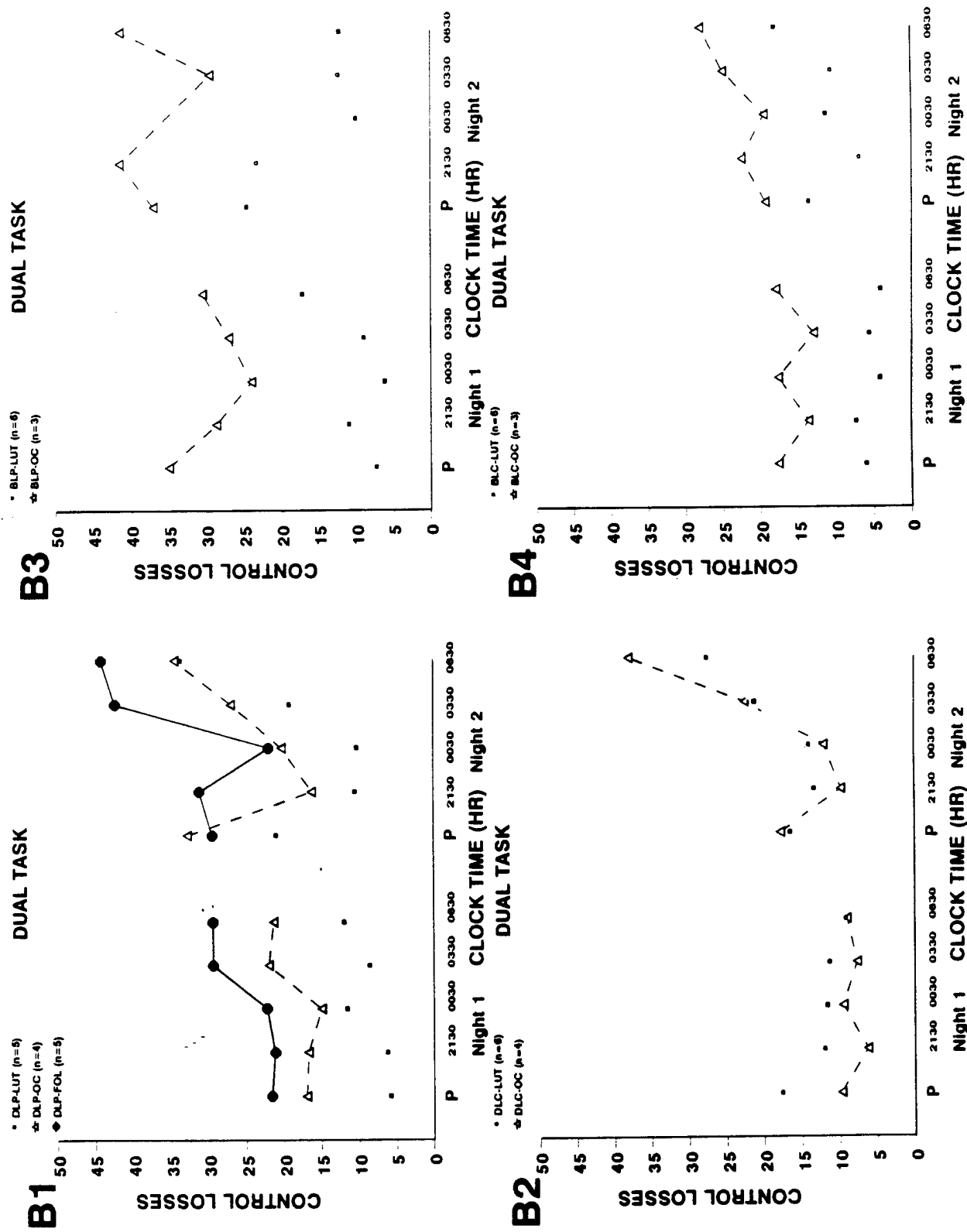


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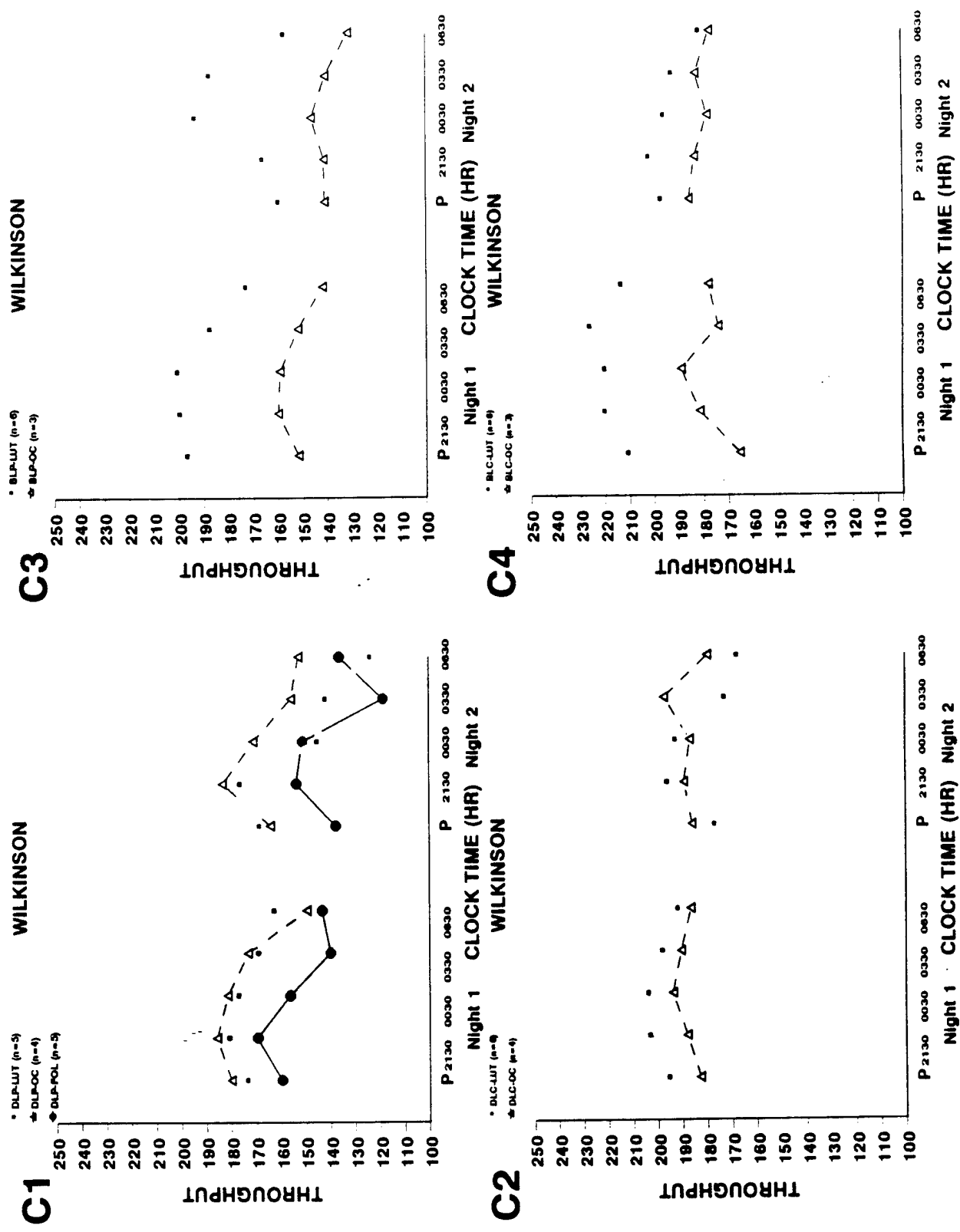


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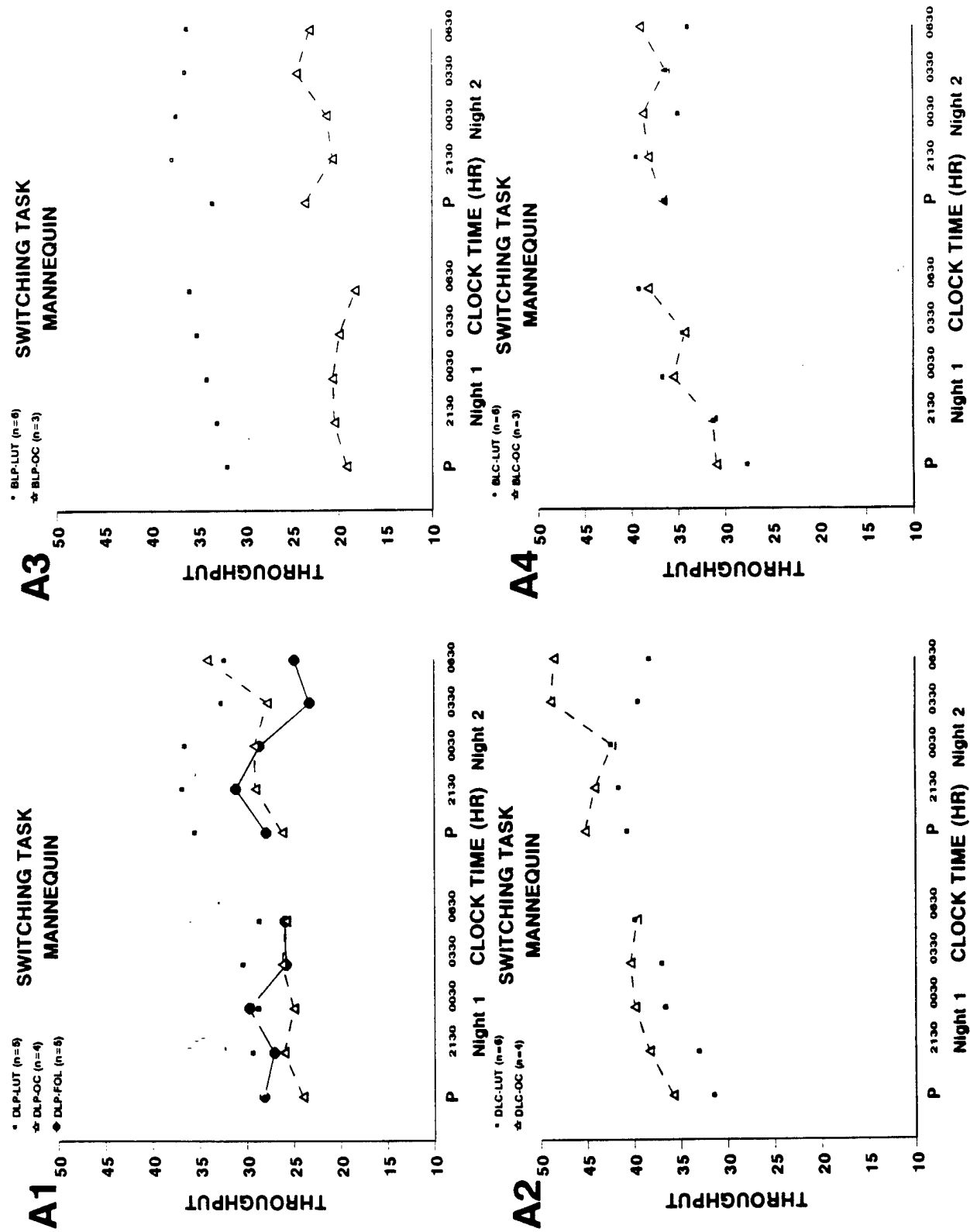


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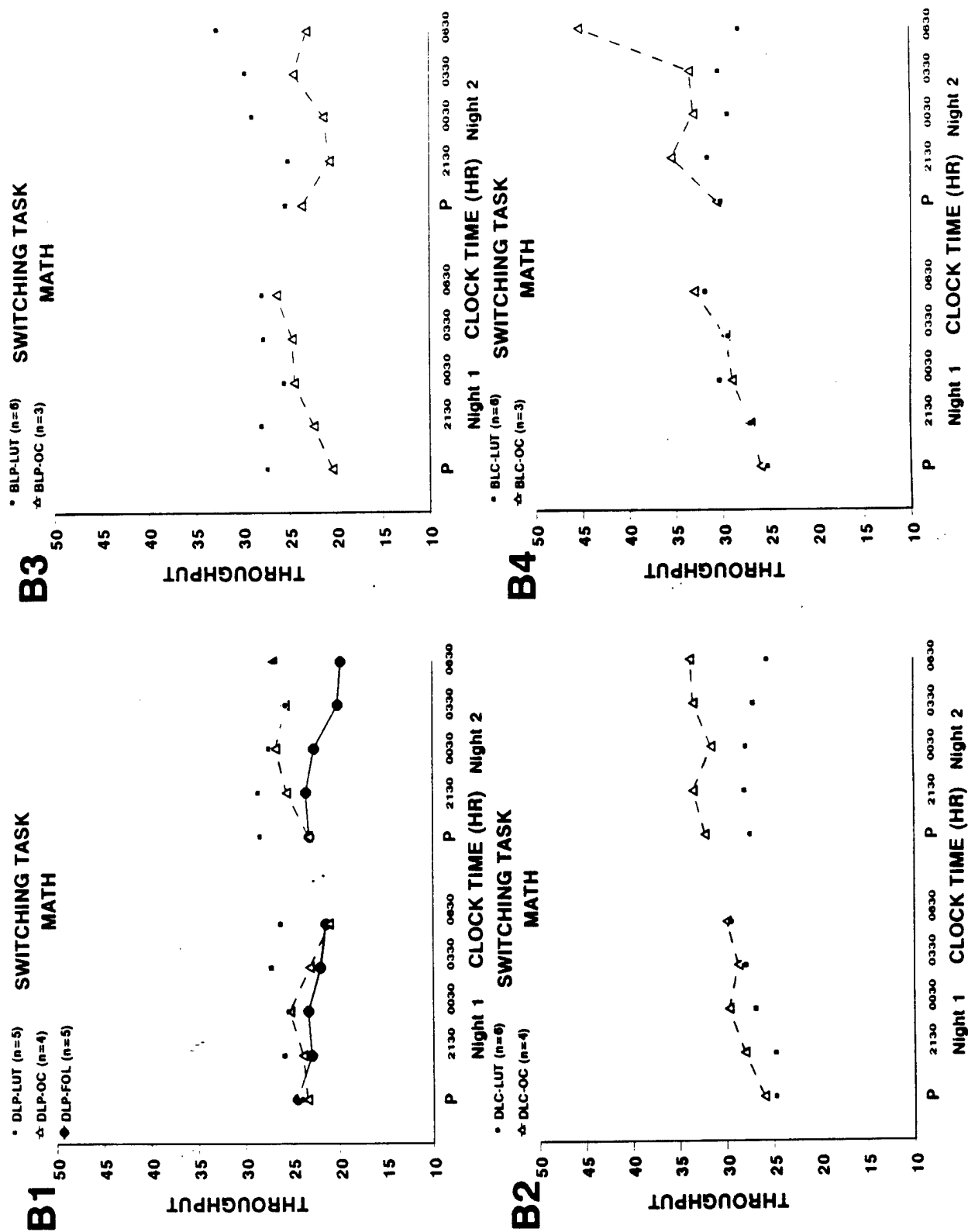


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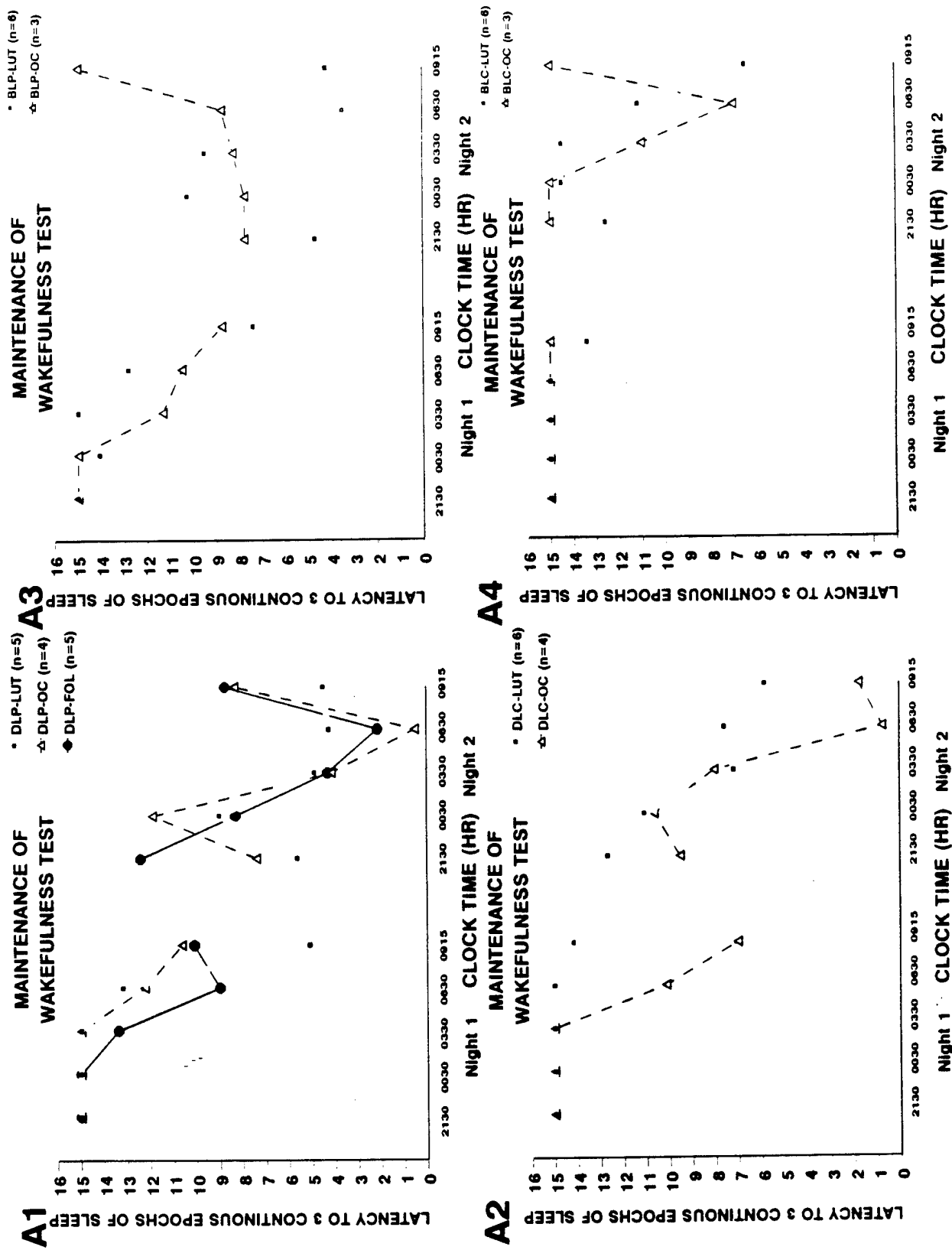


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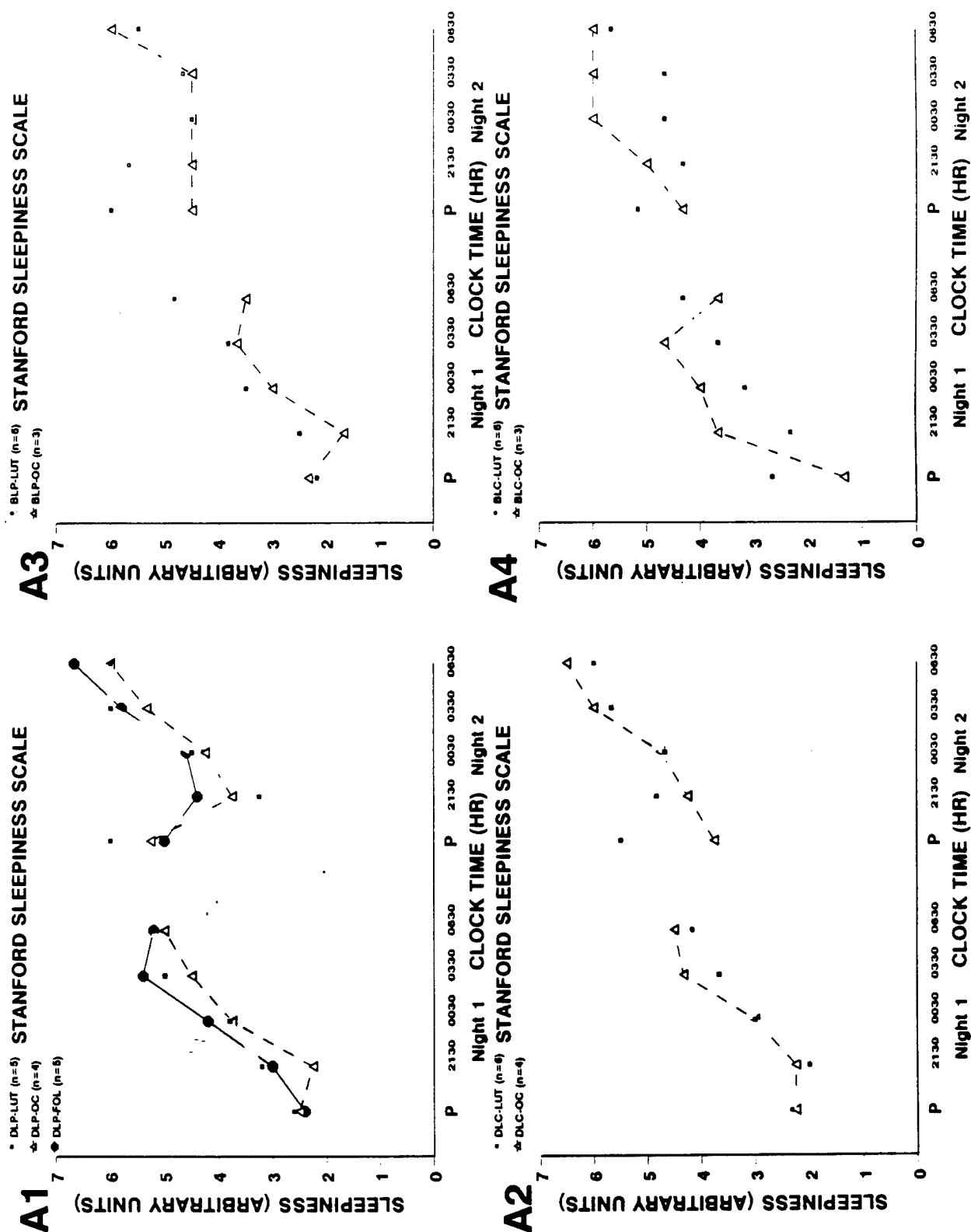


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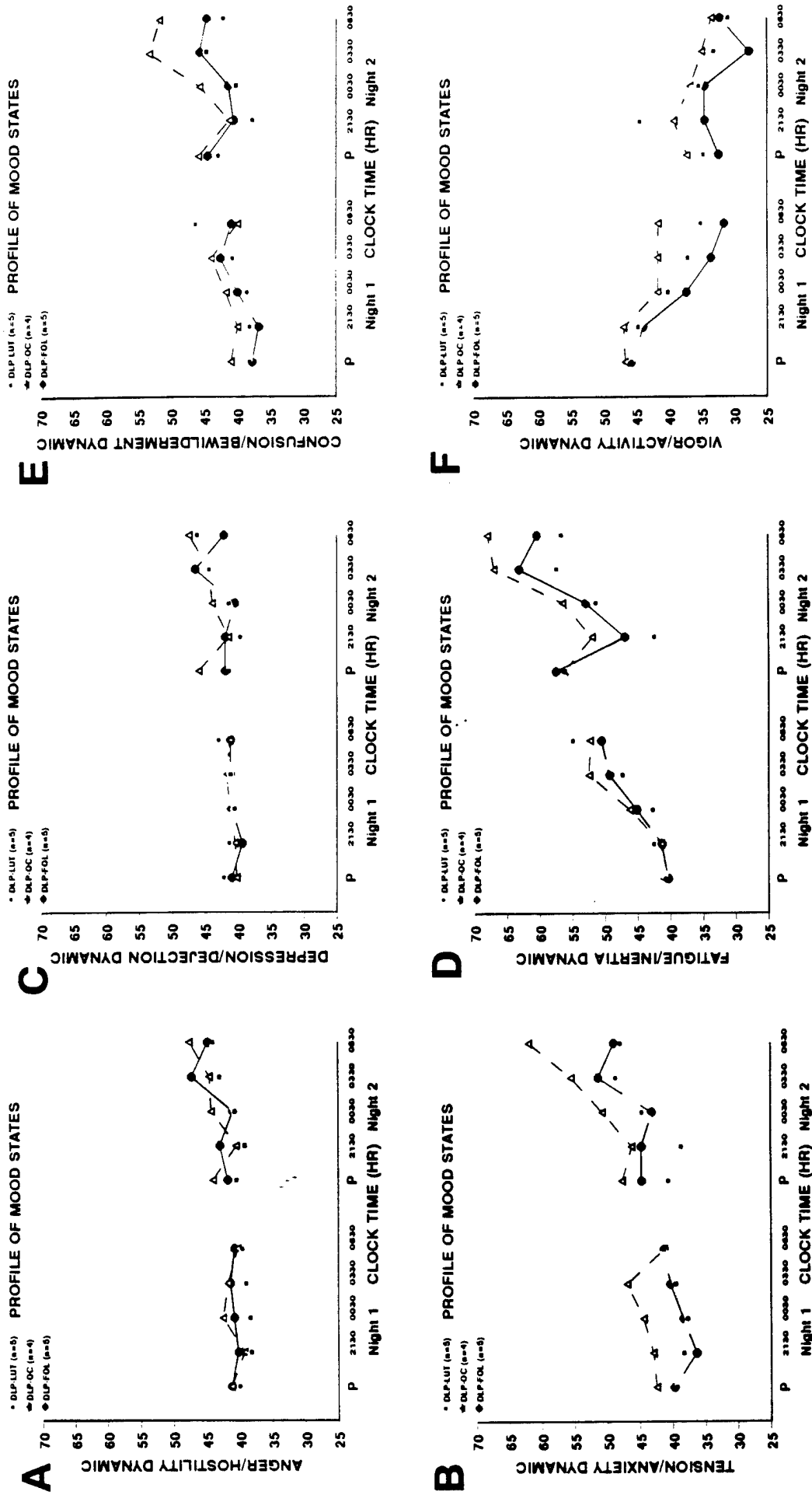


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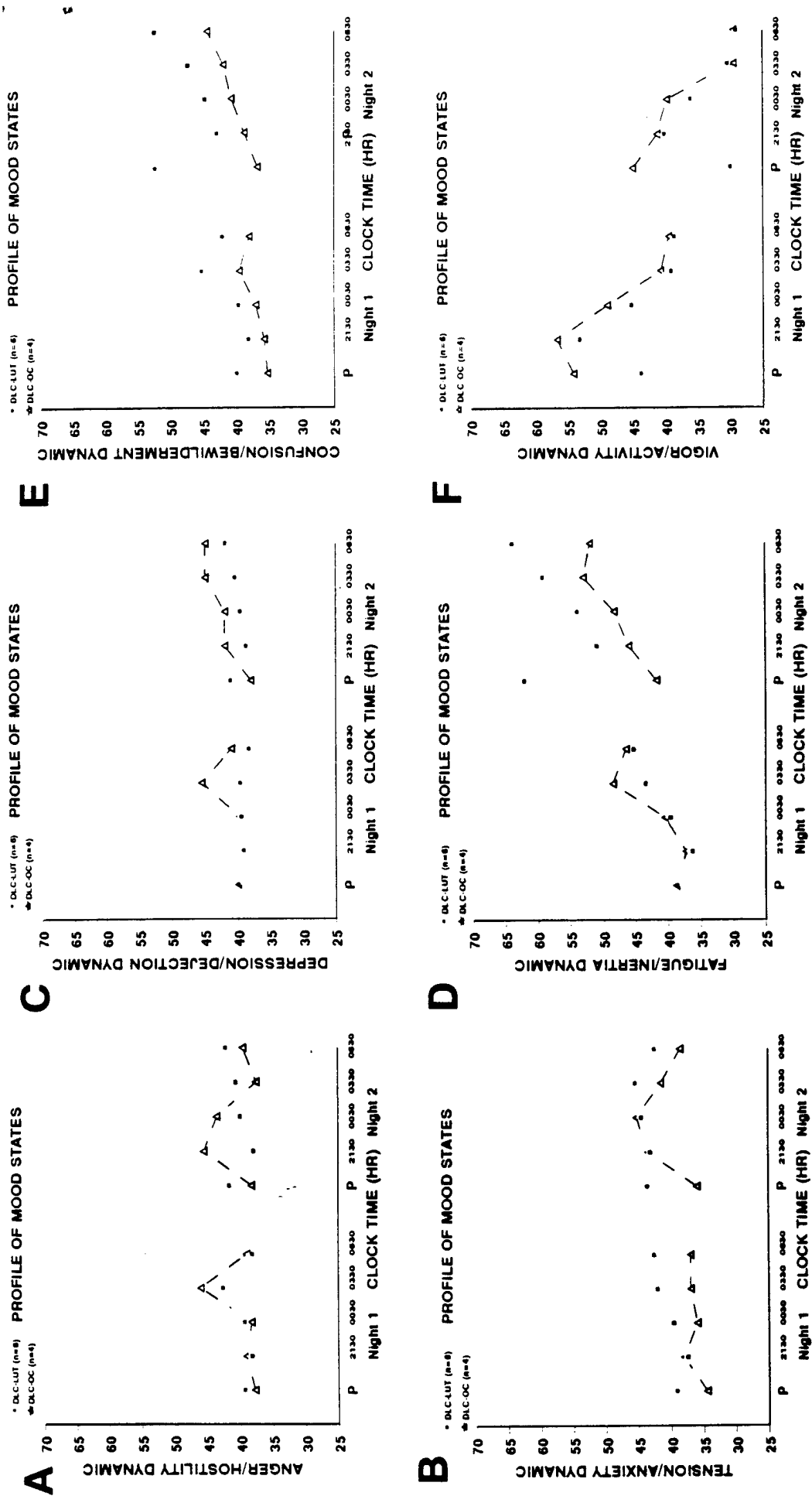


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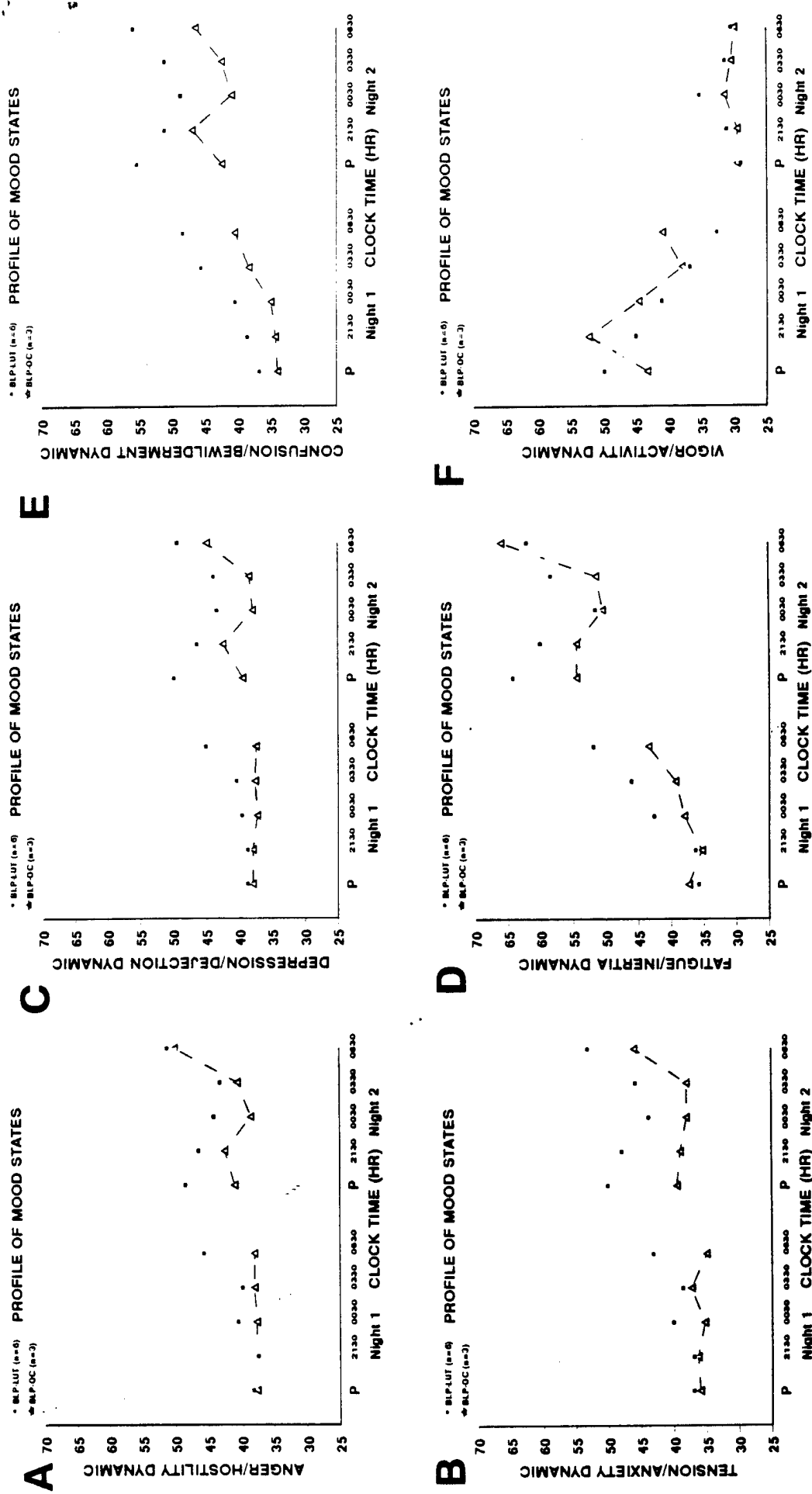


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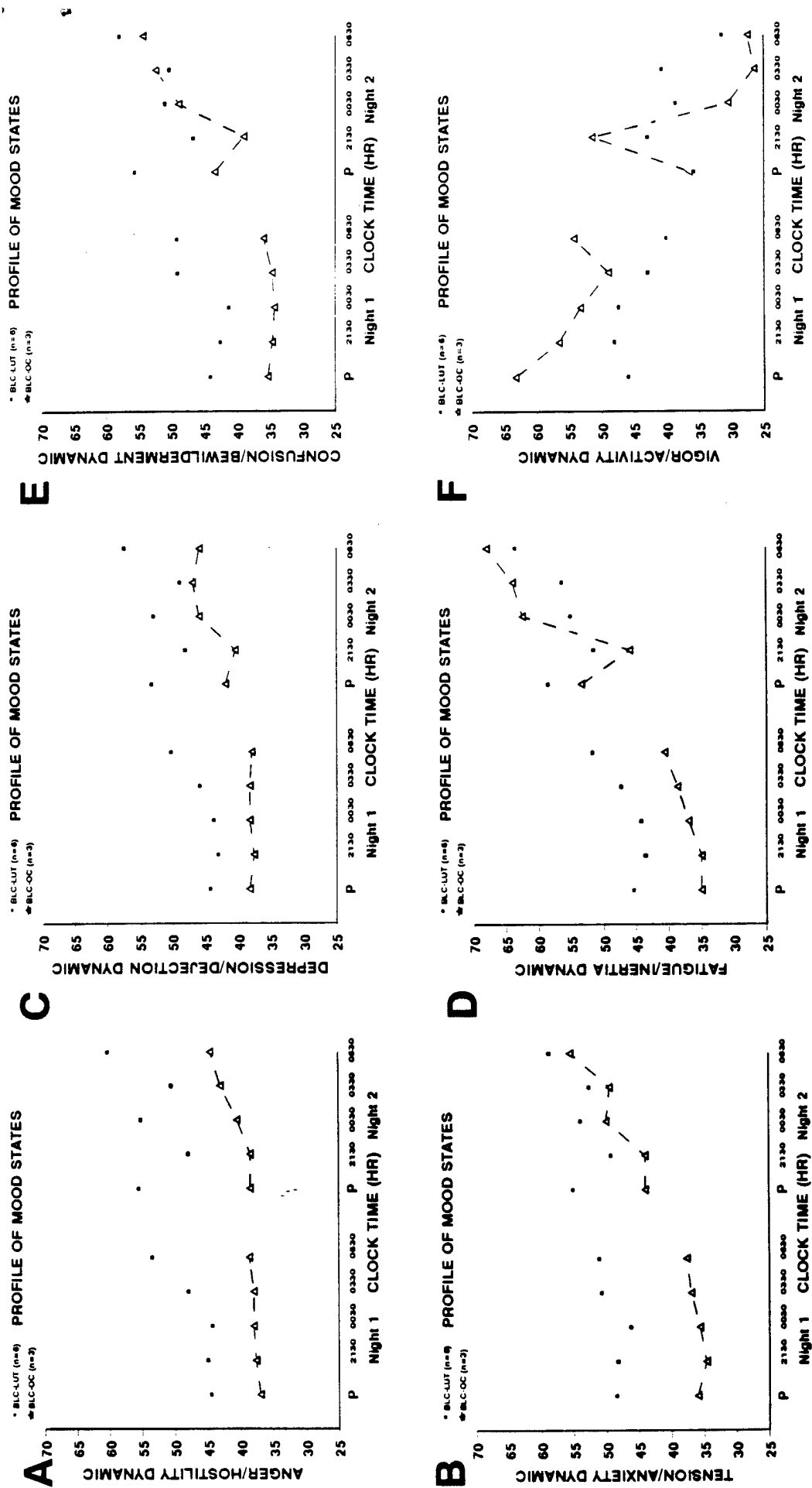


Figure B21(d)

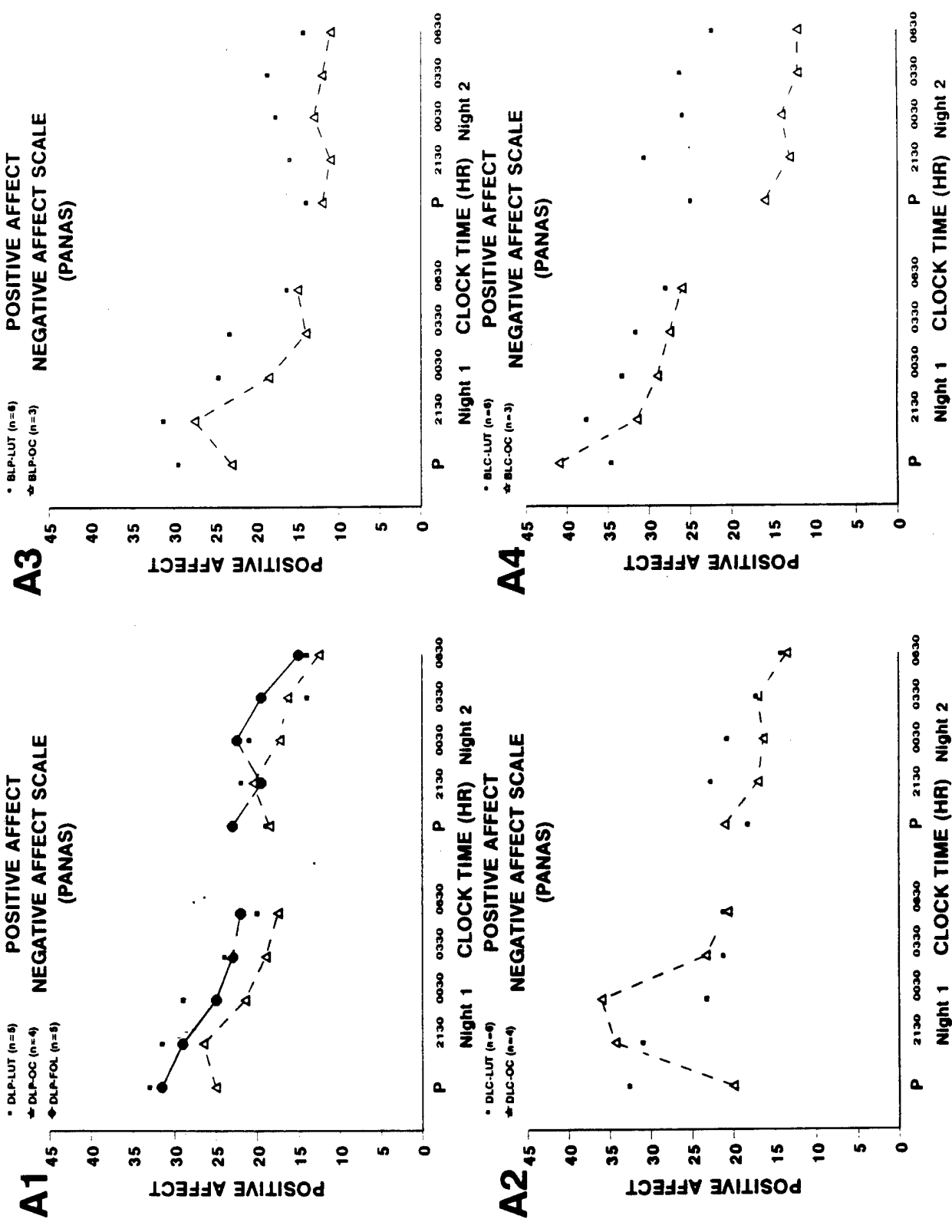


Figure B22(a)

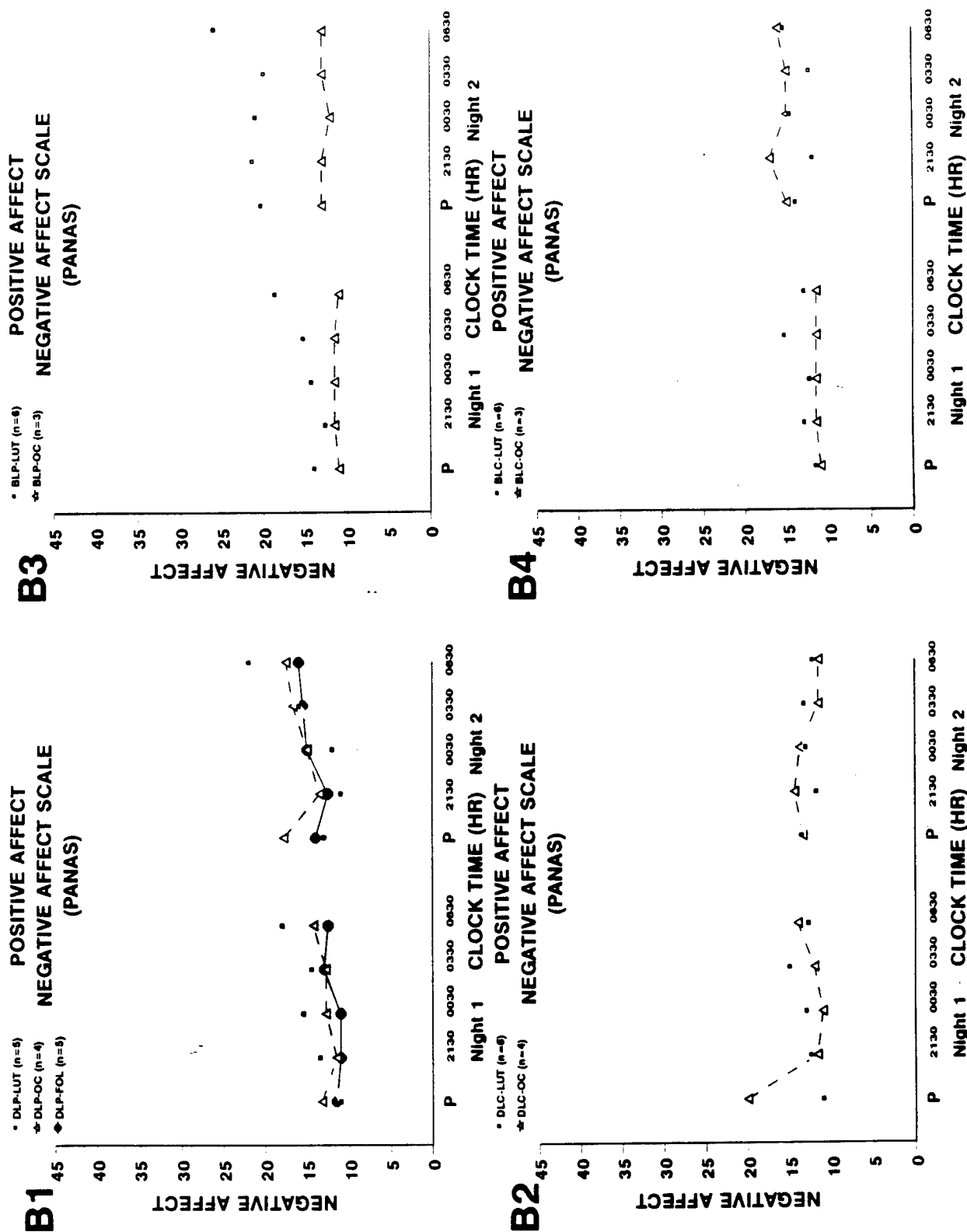


Figure B22(b)

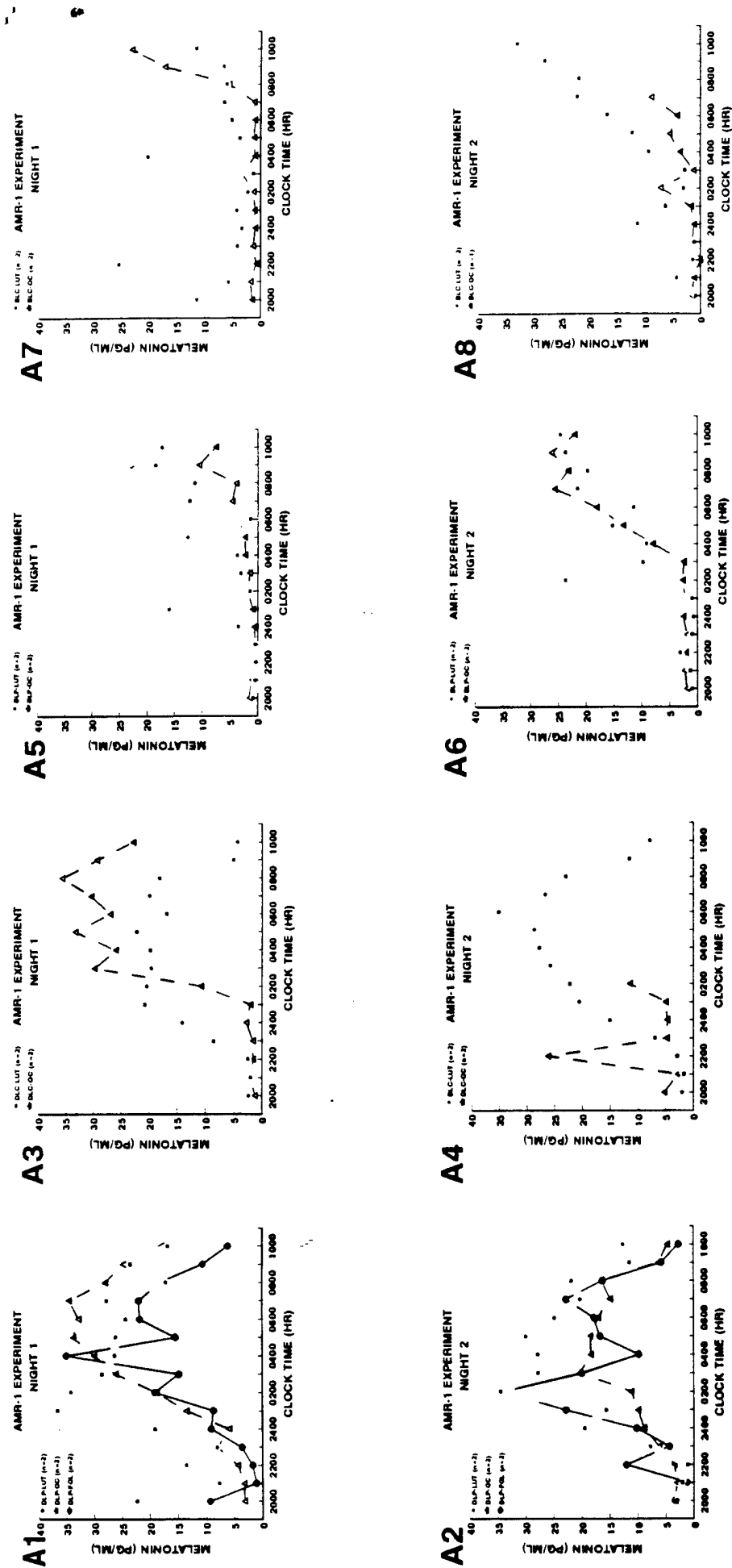


Figure B23:

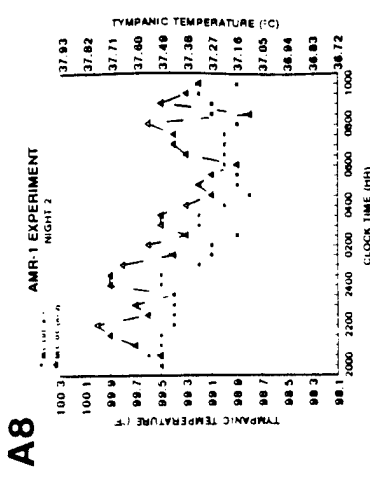
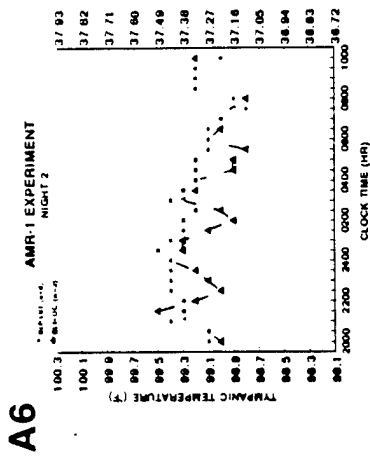
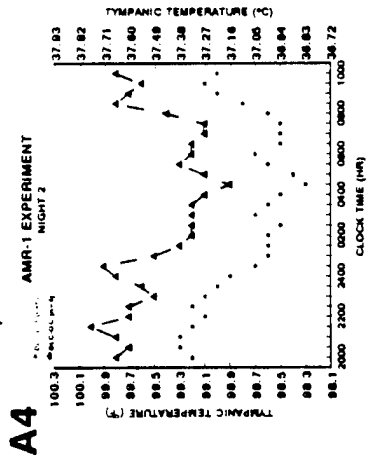
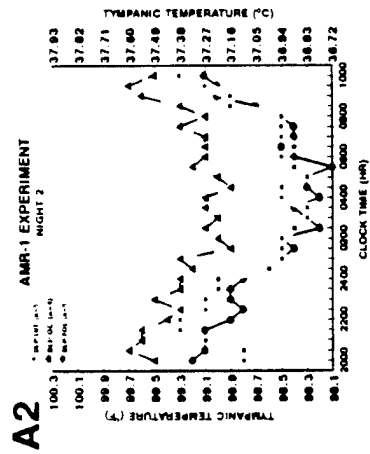
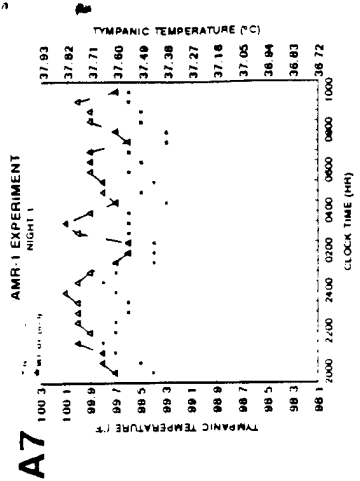
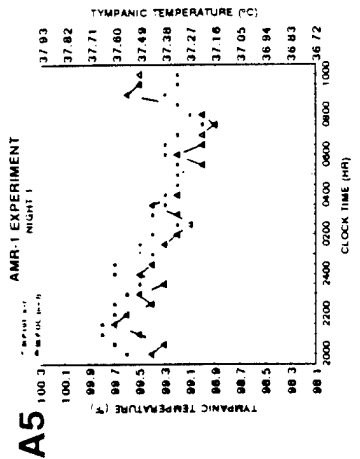
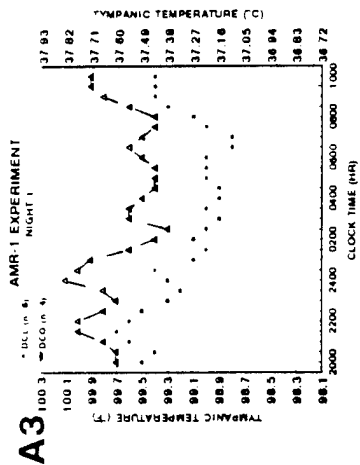
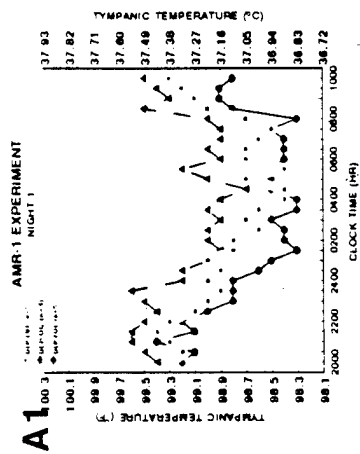


Figure B24